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Sarah Caroline Brown

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Human(wt) parvovirus

parvovirus VP1 protein, parvovirus VP2 protein

parvovirus B19

VACCINE

expression in baculovirus

Spodoptera frugiperdaexpression in other cells - E. coliparvovirus <sup>GNA</sup> ~~particle~~ particle or virus-like particleFusion ~~(p)~~ VP1 or VP2.

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SCHERCHIA OR COLI)/IA  
L9 12 SEA FILE=CA L7 AND L8  
L10 29 SEA FILE=CA (VP1 OR VP2 OR VP(W)(1 OR 2))/IA AND L7  
L11 33899 SEA FILE=CA (VACCIN? OR IMMUNIZ? OR IMMUNIS?)/IA  
L12 12 SEA FILE=CA L7 AND L11  
L13 7 SEA FILE=CA L7 AND BACULOVIR?/IA  
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L19 23 SEA FILE=CA L18 NOT L17

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L15 ANSWER 1 OF 27 COPYRIGHT 1992 ACS  
CA117(19):189741r Immunogenicity studies of recombinant \*\*\*human\*\*\*  
\*\*\*parvovirus\*\*\* \*\*\*B19\*\*\* proteins. Bansal, Geetha P.;  
Hatfield, Jacqueline A.; Dunn, Frances E.; Warrenner, Paul; Young,  
James F.; Top, Franklin H., Jr.; Collett, Marc S.; Anderson, Stacie;  
Rosenfeld, Stephen; et al. (Medimmune, Inc., Gaithersburg, MD 20878,  
USA). Vaccines 92: Mod. Approaches New Vaccines Incl. Prev. AIDS  
[Annu. Meet.], 9th, 315-19. Edited by: Brown, Fred. Cold Spring  
Harbor Lab. Press: Cold Spring Harbor, N. Y. (Eng) 1992. CODEN:  
57WXAL.

AB The B19 empty capsid particles produced in the recombinant  
\*\*\*baculovirus\*\*\* /insect cell system represent potential  
\*\*\*vaccine\*\*\* candidates for \*\*\*human\*\*\* \*\*\*parvovirus\*\*\*  
\*\*\*B19\*\*\* infection. The immunogenicity data have also revealed  
several important pieces of information regarding not only the  
requirements of a suitable \*\*\*vaccine\*\*\* immunogen, but also of

the B19 capsid structure. Antisera to the unique region of VP1 (anti-croVP1-227) recognized intact recombinant empty capsid particles composed of both VP1 and VP2. These sera were also able to neutralize virus infectivity in vitro, indicating that the region unique to the VP1 capsid protein itself possesses virus neutralization (VN) epitopes. Also, at least a portion of the N terminus of the VP1 protein is located on the virion surface. The crit. importance of the VP1 unique region, and antibodies directed against it, was further suggested by a possible correlation between VP1 unique region reactivity and VN. No correlation between ELISA and VN was obsd. The VP1 protein appears to be necessary in empty capsids to create an immunogen capable of eliciting VN antibodies. Whereas the VP1 protein possesses VN epitopes, neutralizing determinants have also been identified within the VP2 protein. That VP2-only capsids failed to elicit VN antibodies may indicate that, in addn. to displaying its own unique VN epitopes, the VP1 protein in capsid particles may cause conformational alterations that either expose or stabilize VN determinants on VP2. Thus, the VP1 protein, or its unique region, alone or in conjunction with capsid particles, will be an essential component of any \*\*\*human\*\*\*  
 \*\*\*parvovirus\*\*\*      \*\*\*B19\*\*\*      \*\*\*vaccine\*\*\* .

L15 ANSWER 2 OF 27 COPYRIGHT 1992 ACS

CA117(9):90791v Applications for peptides found with solid phase synthesis. Fridell, E.; Ruden, U.; Linde, A.; Wahren, B. (Dep. Virol., Karolinska Inst., Stockholm, Swed.). Pept.: Chem. Biol., Proc. Am. Pept. Symp., 12th, Meeting Date 1991, 578-9. Edited by: Smith, John A.; Rivier, Jean E. ESCOM: Leiden, Neth. (Eng) 1992. CODEN: 57XGA9.

AB A report from a symposium on the \*\*\*immunization\*\*\* of rabbits with JB50 and JB151 peptides from B19 \*\*\*human\*\*\*  
 \*\*\*parvovirus\*\*\* , the cause of erythema infectiosum. Antibodies to JB151 appeared rapidly and in all animals \*\*\*immunized\*\*\* . Antibodies to JB50 appeared in some rabbits to a low degree, and were not detected in one rabbit. Booster doses with both peptides promptly provoked titer rises in animals responding well to the \*\*\*immunizations\*\*\* .

L15 ANSWER 3 OF 27 COPYRIGHT 1992 ACS

CA117(7):65078K Unique region of the minor capsid protein of \*\*\*human\*\*\*      \*\*\*parvovirus\*\*\*      \*\*\*B19\*\*\* is exposed on the virion surface. Rosenfeld, Stephen J.; Yoshimoto, Kohji; Kajigaya, Sachiko; Anderson, Stacie; Young, Neal S.; Field, Anne; Warrenner, Paul; Bansal, Geetha; Collett, Marc S. (Cell Biol. Sect., Natl. Heart, Lung and Blood Inst., Bethesda, MD 20817, USA). J. Clin. Invest., 89(6), 2023-9 (Eng) 1992. CODEN: JCINAO. ISSN: 0021-9738.

AB Capsids of the \*\*\*B19\*\*\*      \*\*\*parvovirus\*\*\* are composed of major (VP2; 58 kD) and minor (VP1; 83 kD) structural proteins. These proteins are identical except for a unique 226 amino acid region at the amino terminus of VP1. Previous \*\*\*immunization\*\*\* studies with recombinant empty capsids have demonstrated that the presence of VP1 was required to elicit virus-neutralizing antibody activity. However, to date, neutralizing epitopes have been identified only on VP2. Crystallog. studies of a related parvovirus (canine parvovirus) suggested the unique amino-terminal portion of VP1 assumed an internal position within the viral capsid. To det. the position of VP1 in both empty capsids and virions, a fusion protein contg. the unique region of VP1 was expressed. Antisera raised to this protein recognized recombinant empty capsids contg. VP1 and VP2, but not those contg. VP2 alone, in an ELISA. The antisera immunopptd. both recombinant empty capsids and human plasma-derived virions, and agglutinated the latter as shown by immune electron microscopy. The sera contained potent neutralizing activity for virus infectivity in vitro. These data indicate that a portion of the amino terminus of VP1 is located on the virion surface, and this region contains intrinsic neutralizing determinants. The external location of the

L15 ANSWER 4 OF 27 COPYRIGHT 1992 ACS

CA116(17):171786d Prokaryotic expression of a VP1 polypeptide antigen for diagnosis by a \*\*\*human\*\*\* \*\*\*parvovirus\*\*\* \*\*\*B19\*\*\* antibody enzyme immunoassay. Soderlund, Maria; Brown, Kevin E.; Meurman, Olli; Hedman, Klaus (Dep. Virol., Univ. Helsinki, Helsinki SF-00290, Finland). J. Clin. Microbiol., 30(2), 305-11 (Eng) 1992. CODEN: JCMIDW. ISSN: 0095-1137.

AB To produce \*\*\*parvovirus\*\*\* \*\*\*B19\*\*\* antigen for diagnostic purposes, partially overlapping segments covering the genes encoding the viral structural proteins VP1 and VP2 were cloned into expression vectors. The constructs were induced in Escherichia \*\*\*coli\*\*\*, resulting in the expression of .beta.-galactosidase fusion proteins. In immunoblotting expts. with sera from patients with erythema infectiosum, IgG and IgM antibodies bound to a single polypeptide of 235 amino acids at the N-terminus of VP1. The DNA fragment encoding this polypeptide was amplified by the polymerase chain reaction and cloned into an expression vector. The viral capsid antigen expressed in E. \*\*\*coli\*\*\* was purified by preparative agarose gel electrophoresis and used in IgG and IgM solid-phase enzyme immunoassays. Comparison with ref. .gamma.- and .mu.-capture RIAs using whole virus antigen showed that these antibody tests are suitable for the serodiagnosis of human infection caused by \*\*\*parvovirus\*\*\* \*\*\*B19\*\*\* .

L15 ANSWER 5 OF 27 COPYRIGHT 1992 ACS

CA116(3):19653a Immunogenic peptides of \*\*\*parvovirus\*\*\* \*\*\*B19\*\*\* . Soutschek, Erwin; Motz, Manfred (Mikrogen Molekularbiologische Entwicklungs-G.m.b.H., Germany). Ger. Offen. DE 4003826 A1 14 Aug 1991, 21 pp. (Ger). CODEN: GWXXBX. CLASS: ICM: C07K013-00. ICA: C07K003-20; C07K003-22; B01D015-00; C12N015-62; C12N015-56; C12N015-54. APPLICATION: DE 90-4003826 8 Feb 1990.

AB The title peptides, preferably contg. 8-50 amino acids, contain at least part of the amino acid sequence of the UP1 or UP2 capsid protein of \*\*\*parvovirus\*\*\* \*\*\*B19\*\*\* . They are used for detection of antibodies to B19 and for \*\*\*vaccines\*\*\* . Mol. cloning of VP1 and VP2, and isolation of various fragments, is presented. Amino acid sequences of the fragments are given. Synthetic peptides are also described.

L15 ANSWER 6 OF 27 COPYRIGHT 1992 ACS

CA116(1):4844q A second neutralizing epitope of \*\*\*B19\*\*\* \*\*\*parvovirus\*\*\* implicates the spike region in the immune response. Yoshimoto, Kohji; Rosenfeld, Stephen; Frickhofen, Norbert; Kennedy, Douglas; Hills, Robert; Kajigaya, Sachiko; Young, Neal S. (Cell Biol. Sect., Natl. Heart, Lung, Blood Inst., Bethesda, MD 20892, USA). J. Virol., 65(12), 7056-60 (Eng) 1991. CODEN: JOVIAM. ISSN: 0022-538X.

AB The authors used 18 monoclonal antibodies against \*\*\*B19\*\*\* \*\*\*parvovirus\*\*\* to identify neutralizing epitopes on the viral capsid. Of the 18 antibodies, 9 had in vitro neutralizing activity in a bone marrow colony culture assay. The overlapping polypeptide fragments spanning the B19 structural proteins were produced in a pMAL-c Escherichia \*\*\*coli\*\*\* expression system and used to investigate the binding sites of the neutralizing antibodies. One of the nine neutralizing antibodies reacted with both VP1 and VP2 capsid proteins and a single polypeptide fragment on an immunoblot, identifying a linear neutralizing epitope between amino acids 57 and 77 of the VP2 capsid protein. Eight of nine neutralizing antibodies failed to react with either of the capsid proteins or any polypeptide fragments, despite reactivities with intact virions in a RIA, suggesting that addnl. conformationally dependent neutralizing epitopes exist.

CA115(21):230341j Serological peptides and antibodies to them for diagnosis and protection from infection with B19 virus. Frenzel, Bernd; Roenspeck, Wolfgang (Biochrom Beteiligungs G.m.b.H. und Co., Fed. Rep. Ger.). Ger. Offen. DE 3939470 A1 6 Jun 1991, 5 pp. (Ger). CODEN: GWXXBX. CLASS: ICM: C07K007-10. ICS: A61K039-12; A61K049-00; G01N033-68. APPLICATION: DE 89-3939470 29 Nov 1989.

AB Peptides are provided which are useful as \*\*\*vaccines\*\*\* against infection with \*\*\*human\*\*\* \*\*\*parvovirus\*\*\* \*\*\*B19\*\*\* (the causative agent of infectious erythema), or diagnostically for detection of antibodies to the virus. Thus, in an ELISA and anti-B19 antibodies in serum, the B19-specific peptide, Ala-Ala-Ser-Ser-Cys-His-Asn-Ala-Ser-Gly-Lys-Glu-Ala-Lys-Val-Gly-Thr-Ile-Ser-Pro-Ile-Met-Gly-Tyr-Ser-Thr-Pro-Trp, was adsorbed onto a microtiter plate, incubated with the test serum, and then incubated with peroxidase-labeled antibody to human IgG. The same peptide was also conjugated to keyhole limpet hemocyanin and used to elicit antibodies in sheep for use in an ELISA for detection of the B19 antigen.

CA115(15):154634q Preliminary x-ray crystallographic investigation of \*\*\*human\*\*\* \*\*\*parvovirus\*\*\* \*\*\*B19\*\*\*. Agbandje, Mavis; McKenna, Robert; Rossmann, Michael G.; Kajigaya, Sachiko; Young, Neal S. (Dep. Biol. Sci., Purdue Univ., West Lafayette, IN 47907, USA). Virology, 184(1), 170-4 (Eng) 1991. CODEN: VIRLAX. ISSN: 0042-6822.

AB Crystals that diffract x rays to at least 8 .ANG. resolu. were grown from human \*\*\*B19\*\*\* \*\*\*parvovirus\*\*\* empty capsids. These particles consist of VP-2 derived from a \*\*\*baculovirus\*\*\* expression system. This is possibly the first time that a self-assembled empty viral capsid, grown in other than normal host cells, has been crystd. Partial x-ray diffraction data have been collected using synchrotron radiation. The space group is P213 with a = 362 .ANG.. The particle position in the crystal cell is given, at least roughly, from packing considerations.

CA115(13):133520j Self-assembled \*\*\*B19\*\*\* \*\*\*parvovirus\*\*\* capsids, produced in a \*\*\*baculovirus\*\*\* system, are antigenically and immunogenically similar to native virions. Kajigaya, Sachiko; Fujii, Hiroyuki; Field, Anne; Anderson, Stacie; Rosenfeld, Stephen; Anderson, Larry J.; Shimada, Takashi; Young, Neal S. (Clin. Hematol. Branch, Natl. Heart, Lung, Blood Inst., Bethesda, MD 20892, USA). Proc. Natl. Acad. Sci. U. S. A., 88(11), 4646-50 (Eng) 1991. CODEN: PNASA6. ISSN: 0027-8424.

AB \*\*\*B19\*\*\* \*\*\*parvovirus\*\*\* is pathogenic in humans, causing fifth disease, transient aplastic crisis, some cases of hydrops fetalis, and acquired pure red cell aplasia. Efforts to develop serol. assays and \*\*\*vaccine\*\*\* development have been hampered by the virus's extreme tropism for human bone marrow and the absence of a convenient culture system. Recombinants were constructed contg. either the major (VP2) or minor (VP1) structural proteins of B19 in a \*\*\*baculovirus\*\*\* -based plasmid, from which the polyhedrin gene had been deleted; these recombinant plasmids were used to generate recombinant infectious \*\*\*baculovirus\*\*\*. Subsequent infection of insect cells in vitro resulted in high-level expression of either B19VP1 or VP2. Parvovirus capsids were obtained by self-assembly in cell cultures coinfectd with either VP1- and VP2-contg. \*\*\*baculoviruses\*\*\* or, surprisingly, VP2-contg. \*\*\*baculoviruses\*\*\* alone. Empty B19 capsids composed of VP1 and VP2 could replace serumvirus as a source of antigen in a conventional immunoassay for detection of either IgG or IgM antiparvovirus antibodies in human serum. \*\*\*Immunization\*\*\* of rabbits with capsids composed of VP1 and VP2 resulted in prodn. of

antiserum that recognized serum parvovirus on immunoblot and neutralized parvovirus infectivity for human erythroid progenitor cells. Thus, \*\*\*baculovirus\*\*\* -derived parvovirus antigen can substitute for scarce viral antigen in immunoassays and should be suitable as a human \*\*\*vaccine\*\*\*.

L15 ANSWER 10 OF 27 COPYRIGHT 1992 ACS

CA115(3):23704q \*\*\*Human\*\*\* \*\*\*parvovirus\*\*\* \*\*\*b19\*\*\* proteins and virus-like particles; their recombinant manufacture and use in diagnostic assays and \*\*\*vaccines\*\*\*. Brown, Caroline Sarah (Rijksuniversiteit Leiden, Neth.). PCT Int. Appl. WO 9104330 A1 4 Apr 1991, 30 pp. DESIGNATED STATES: W: US; RW: AT, BE, CH, DE, DK, ES, FR, GB, IT, LU, NL, SE. (Eng). CODEN: PIXXD2. CLASS: ICM: C12N015-35. ICS: C12N005-10; C12P021-02; C12N015-86; G01N033-569; A61K039-23; A61K039-295. APPLICATION: WO 90-NL130 11 Sep 1990. PRIORITY: NL 89-2301 14 Sep 1989.

AB The proteins VP1 and VP2 of the \*\*\*human\*\*\* \*\*\*parvovirus\*\*\* \*\*\*B19\*\*\* are manufd. for use in \*\*\*vaccines\*\*\* and diagnostics by expression of the genes in Sf9 cells using a \*\*\*baculovirus\*\*\* expression system. The genes encoding these proteins were cloned in Autographa californica nuclear polyhedrosis virus by std. methods to give the recombinant viruses AcB19VP1L and AcR19VP1L. The protein was produced in high yields and was stable when the genes were expressed in Sf9 cells. Cells expressing Mes gene were useful for detection of antibody to the protein in serum samples. Cells expressing the gene for either VP1 or VP2 protein or both accumulated particles that resemble the virus.

L15 ANSWER 11 OF 27 COPYRIGHT 1992 ACS

CA114(25):241883t Expression of an antigenic polypeptide of the \*\*\*human\*\*\* \*\*\*parvovirus\*\*\* \*\*\*B19\*\*\*. Eiffert, H.; Koechel, H. G.; Heuer, M.; Tratschin, J. D.; Thomssen, R. (Cent. Hyg. Hum. Genet., Georg-August-Univ., Goettingen D-3400, Fed. Rep. Ger.). ~~Med. Microbiol. Immunol., 179(4), 163-75, (Eng), 1990.~~ CODEN: MMIYAO. ISSN: 0300-8584.

AB The DNA fragment of the \*\*\*human\*\*\* \*\*\*parvovirus\*\*\* \*\*\*B19\*\*\*, with 715 nucleotides between nucleotide positions 3141-3856 was expressed in Escherichia \*\*\*coli\*\*\* as a .beta.-galactosidase fusion protein. The plasmid vector pSS20d used for this purpose permits cleavage of the viral gene product from the .beta.-galactosidase moiety by collagenase. After purifn. by p-aminophenyl-.beta.-D-thiogalactoside-sepharose and superose, a sol. protein with a mol. mass of 28 kDa was isolated. It represents a common part of the viral capsid proteins VP1 and VP2. This bacterially derived parvoviral gene product can be used for detection of anti-B19 antibodies in human sera.

L15 ANSWER 12 OF 27 COPYRIGHT 1992 ACS

CA114(21):201047s Assembly of empty capsids by using \*\*\*baculovirus\*\*\* recombinants expressing \*\*\*human\*\*\* \*\*\*parvovirus\*\*\* \*\*\*B19\*\*\* structural proteins. Brown, Caroline S.; Van Lent, Jan W. M.; Vlak, Just M.; Spaan, Willy J. M. (Fac. Med., Leiden Univ., Leiden 2300 AH, Neth.). J. Virol., 65(5), 2702-6 (Eng) 1991. CODEN: JOVIAM. ISSN: 0022-538X.

AB Empty \*\*\*parvovirus\*\*\* \*\*\*B19\*\*\* capsids were isolated from insect cells infected with a recombinant \*\*\*baculovirus\*\*\* expressing \*\*\*parvovirus\*\*\* \*\*\*B19\*\*\* VP2 alone and also with a double-recombinant \*\*\*baculovirus\*\*\* expressing both VP1 and VP2. That VP2 alone can assemble to form capsids is a novel phenomenon in parvoviruses. The stoichiometry of the capsids contg. both VP1 and VP2 was similar to that previously obsd. in \*\*\*parvovirus\*\*\* \*\*\*B19\*\*\* -infected cells. The capsids were similar to native capsids in size and appearance, and their antigenicity was demonstrated by immunopptn. and enzyme-like immunosorbent assay with B19-specific antibodies.

CA114(17):164821s New \*\*\*human\*\*\* \*\*\*parvovirus\*\*\* peptides with disulfide bridge for \*\*\*immunization\*\*\* or diagnosis. Trojnar, Jerzy; Wahren, Britta; Fridell, Eva (Ferring Diagnostica AB, Swed.). PCT Int. Appl. WO 9013567 A1 15 Nov 1990, 19 pp. DESIGNATED STATES: W: AU, CA, FI, JP, KR, NO, US; RW: AT, BE, CH, DE, DK, ES, FR, GB, IT, LU, NL, SE. (Eng). CODEN: PIXXD2. CLASS: ICM: C07K007-10. ICS: G01N033-569; A61K039-23. APPLICATION: WO 90-SE276 25 Apr 1990. PRIORITY: SE 89-1566 28 Apr 1989.

AB The title peptides (I and II), having an amino acid sequence corresponding to an epitope of a \*\*\*human\*\*\* \*\*\*parvovirus\*\*\* and further having 2 Cys residues located on each side of the epitope and a disulfide bond between the 2 Cys residues, were prep'd. by the solid phase method on a 4-methylbenzhydrylamine resin. The disulfide bond stabilizes the peptides and enhance the antibody binding activity as well as their chem. stability. I and II are useful as antigens for diagnostic immunoassay of or \*\*\*vaccines\*\*\* against a \*\*\*human\*\*\* \*\*\*parvovirus\*\*\* (no data).

CA114(3):18831d The production of \*\*\*human\*\*\* \*\*\*parvovirus\*\*\* capsid proteins in Escherichia \*\*\*coli\*\*\* and their potential as diagnostic antigens. Rayment, F. B.; Crosdale, E.; Morris, D. J.; Pattison, J. R.; Talbot, P.; Clare, J. J. (Dep. Mol. Biol., Wellcome Biotech, Beckenham/Kent BR3 3BS, UK). ~~Journal of Virology, 71(4):1065-1072, 1990~~ CODEN: JGVIAV. ISSN: 0022-1317.

AB A no. of polypeptides derived from the capsid proteins of the \*\*\*human\*\*\* \*\*\*parvovirus\*\*\* \*\*\*B19\*\*\* were expressed in E. \*\*\*coli\*\*\*. These include native VP1 (84K) and VP2 (58K) proteins and also fusions to .beta.-galactosidase contg. differing amts. of the amino terminus of the VP1/2 polypeptide. Although each of these was expressed at high levels and the majority were produced as full-length proteins, only one was sol. This sol. polypeptide, p132, is a .beta.-galactosidase fusion protein that includes 145 amino acids from B19 which are entirely derived from the region unique to VP1. Despite contg. such a small portion of VP1, which itself constitutes only 4% of total capsid protein, p132 reacted with all known anti-B19 IgM-pos. human serum samples. This region apparently contains epitopes which must be prominently exposed on the intact virus. The use of this recombinant antigen was in a simple diagnostic assay for B19-specific antibodies which can be used for initial screening of human serum samples. In a survey of 103 serum specimens, ELISA pos. identified all samples (19/19) which were pos. by IgM antibody capture RIA. The recombinant p132 antigen is efficiently produced and readily purified from E. \*\*\*coli\*\*\*, and its use as a diagnostic antigen should increase the availability of routine clin. testing for \*\*\*human\*\*\* \*\*\*parvovirus\*\*\* infection.

CA113(17):150192e An immunofluorescence assay for the detection of \*\*\*parvovirus\*\*\* \*\*\*B19\*\*\* IgG and IgM antibodies based on recombinant viral antigen. Brown, Caroline S.; Van Bussel, Mario J. A. W. M.; Wassenaar, Alfred L. M.; Van Elsacker-Niele, Anne Marie W.; Weiland, Harro T.; Salimans, Marcel M. M. (Fac. Med., Univ. Hosp., Leiden 2300 AH, Neth.). J. Virol. Methods, 29(1), 53-62 (Eng) 1990. CODEN: JVMEHD. ISSN: 0166-0934.

AB An indirect immunofluorescence assay for serum IgG and IgM antibodies to \*\*\*human\*\*\* \*\*\*parvovirus\*\*\* \*\*\*B19\*\*\* was established using recombinant B19 viral antigen, the capsid protein VP1, which had been produced in a \*\*\*baculovirus\*\*\* expression system. This protein gives a strong and characteristic signal in the immunofluorescence assay, making it a suitable candidate for this test system. The test results showed a good correlation with results obtained with a solid-phase capture RIA. The 76% of sera from a random selection of blood donors were pos. for B19 IgG which agrees

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with previous findings. The course of the IgM and IgG antibody response to B19 infection could be followed with the immunofluorescence assay by detg. the titers of series of sera taken after a recent B19 infection. Investigation of sera contg. rubella-specific IgM showed no cross-reactivity with the recombinant B19 VP1 used in this test system.

L15 ANSWER 16 OF 27 COPYRIGHT 1992 ACS

CA113(13):113342h A genetically engineered cell line that produces empty capsids of \*\*\*human\*\*\* \*\*\*parvovirus\*\*\* \*\*\*B19\*\*\* . Kajigaya, Sachiko; Frickhofen, Norbert; Kurtzman, Gary; Shimada, Takashi; Young, Neal S.; Field, Anne (Clin. Hematol. Branch, NHLBI, Bethesda, MD 20892, USA). Vaccines 90: Mod. Approaches New Vaccines Incl. Prev. AIDS, [Conf.], 7th, Meeting Date 1989, 63-8. Edited by: Brown, Fred. Cold Spring Harbor Lab.: Cold Spring Harbor, N. Y. (Eng) 1990. CODEN: 56UPAE.

AB A 3-11-5 cell line that stably produces \*\*\*B19\*\*\* \*\*\*parvovirus\*\*\* empty capsids was established. Empty capsid prodn. is equal to or greater than virion prodn. by infected bone marrow cells, estd. at 1000-2000 capsids/cell. The growth of cells was not diminished by capsid prodn. In capture immunoassay, 3-11-5 lysate was equiv. to serum contg. virus for the detection of IgG and IgM antibodies. This cell line will be useful for the development of clin. anti- \*\*\*B19\*\*\* \*\*\*parvovirus\*\*\* antibody assays, as it should provide an unlimited supply of B19 antigen. The 3-11-5 cells are potentially useful in the development of a \*\*\*vaccine\*\*\* and a packaging cell line for gene therapy.

L15 ANSWER 17 OF 27 COPYRIGHT 1992 ACS

CA113(7):57367f Antigenic \*\*\*parvovirus\*\*\* \*\*\*B19\*\*\* coat proteins VP1 and VP2 produced in large quantities in a \*\*\*baculovirus\*\*\* expression system. Brown, Caroline S.; Salimans, Marcel M. M.; Noteborn, Mathieu H. M.; Weiland, Harro T. (Dep. Virol., Univ. Hosp. Leiden, Leiden 2300 AH, Neth.). Virus Res., 15(3), 197-211 (Eng) 1990. CODEN: VIREDF. ISSN: 0168-1702.

AB Two \*\*\*baculovirus\*\*\* expression vectors derived from Autographa californica nuclear polyhedrosis virus (AcNPV) were prepd. contg. the complete 2.5-kb coding region for \*\*\*parvovirus\*\*\* \*\*\*B19\*\*\* coat protein VP1 (AcB19VP1L) and the 1.8-kb coding region for VP2 (AcB19VP2L), placed under the control of the polyhedrin promoter. The recombinant viruses were used to infect \*\*\*Spodoptera\*\*\* \*\*\*frugiperda\*\*\* cells and the proteins expressed were analyzed using appropriate antibodies. AcB19VP1L-infected cells produced B19 VP1, as shown by its reaction with 13 human sera contg. B19-specific antibodies in Western blot anal. and indirect immunofluorescence. The signal seen with VP1 in immunofluorescence makes it suitable for the development of a diagnostic assay based on this technique. VP1 also reacted with 2 monoclonal antibodies (mAbs) specific for the B19 protein part of a 196 kDa .beta.-galactosidase B19 fusion protein expressed in Escherichia \*\*\*coli\*\*\* . Cells infected with AcB19VP2L produced B19 VP2 which reacted with the same human sera in indirect immunofluorescence and with 5 of the 13 sera in Western blots. VP2 did not react with the fusion protein-specific mAbs. The large amts. of viral antigen produced in this system means the development of widely available diagnostic tests for B19 infection and the further characterization of the B19 structural proteins are within reach.

L15 ANSWER 18 OF 27 COPYRIGHT 1992 ACS

CA112(19):173197d Cloning of the \*\*\*human\*\*\* \*\*\*parvovirus\*\*\* \*\*\*B19\*\*\* genome and structural analysis of its palindromic termini. Deiss, Veronika; Tratschin, Jon Duri; Weitz, Manfred; Siegl, Guenter (Inst. Hyg. Med. Microbiol., Univ. Bern, Bern CH-3010, Switz.). Virology, 175(1), 247-54 (Eng) 1990. CODEN: VIRLAX. ISSN: 0042-6822.

AB The entire 5.6-kb single-stranded DNA genome of the \*\*\*human\*\*\*



\*\*\*parvovirus\*\*\*  
 \*\*\*B19\*\*\* was cloned in bacterial plasmids. Stable amplification of the recombinant plasmid DNA was achieved in Escherichia \*\*\*coli\*\*\* JC8111 but not in HB101 cells. Sequence anal. of the cloned DNA shows that the terminal 383 nucleotides at each end of the genome are identical inverted repeats. The distal 365 nucleotides of the repeat represent an imperfect palindrome which presumably folds over to form a hairpin structure. The sequence of the hairpin occurs in two distinct configurations which are related in that one is the inverted complement of the other. Such alternative configurations of the terminal hairpins have been found for all parvoviruses analyzed so far and are referred to as flip and flop.

L15 ANSWER 19 OF 27 COPYRIGHT 1992 ACS

CA112(3):17314j Expression of the \*\*\*human\*\*\* \*\*\*parvovirus\*\*\* \*\*\*B19\*\*\* protein fused to protein A in Escherichia \*\*\*coli\*\*\* : recognition by IgM and IgG antibodies in human sera. Morinet, F.; D'Auriol, L.; Tratschin, J. D.; Galibert, F. (Centre Hayem, Hop. Saint-Louis, Paris 75010, Fr.). ~~J. Gen. Virol., 70(11), 3091-7 (Eng) 1989~~ CODEN: JGVIAV. ISSN: 0022-1317.

AB A 1.4 kb fragment (nucleotides 2430 to 3901) encoding portions of the \*\*\*human\*\*\* \*\*\*parvovirus\*\*\* \*\*\*B19\*\*\* structural proteins was inserted into the pRIT2 plasmid expression vector contg. the gene encoding staphylococcal Protein A under the control of the phage .lambda. promoter PR. The fusion protein was used to raise antibodies in rabbits. The sera were shown by immune electron microscopy to agglutinate B19 particles and were also shown to recognize the VP2 B19 capsid protein, by Western blot anal. The B19 antigenicity of the fusion protein was confirmed by immunoblot and enzyme immunoassay with IgG and IgM anti-B19-pos. ref. human sera.

L15 ANSWER 20 OF 27 COPYRIGHT 1992 ACS

CA112(1):6051v A genetically engineered cell line that produces empty capsids of B19 ( \*\*\*human\*\*\* ) \*\*\*parvovirus\*\*\* . Kajigaya, Sachiko; Shimada, Takashi; Fujita, Shinsuke; Young, Neal S. (Cell Biol. Sect., Natl. Heart, Lung, Blood Inst., Bethesda, MD 20892, USA). ~~Proc. Natl. Acad. Sci. U. S. A., 86(19), 7601-5 (Eng) 1989~~ CODEN: PNASA6. ISSN: 0027-8424.

AB The right half of the cloned B19 genome and a minigene derived from the human dihydrofolate reductase gene (DHFR) were cotransfected into dhfr- Chinese hamster ovary cells and selected clones were screened by RNA anal.; after amplification in methotrexate, clones were tested for capsid protein expression. A cell line, designated 3-11-5, stably expressed nearly full-length transcripts for the 2 capsid proteins. These cells produced the major and minor structural protein species in natural proportions that self-assembled into virion capsids. Capsids from 3-11-5 cells could be sepd. from virions by sucrose gradient sedimentation and had the d. on CsCl isopycnic sedimentation of empty parvovirus capsids. Capsid protein was present in both nuclei and cytoplasm on immunofluorescence study but fractionated with the cytosol on purifn. Empty capsid prodn. was equal to or greater than virion prodn. by infected bone-marrow cells, 1000-2000 capsids/cell, but cell growth was not diminished by capsid prodn. This cell line will be useful in developing practical assays for \*\*\*B19\*\*\* \*\*\*parvovirus\*\*\* antibody and a \*\*\*vaccine\*\*\* for the virus, as well as potentially serving as a packaging cell line for gene therapy.

\* L15 ANSWER 21 OF 27 COPYRIGHT 1992 ACS

CA111(23):210112z Manufacture of parvovirus capsid proteins and empty capsids in transgenic animal cell culture. Young, N.; Kajigaya, S.; Shimada, T. (United States Dept. of Health and Human Services, USA). U. S. Pat. Appl. US 270098 A0 15 Apr 1989, 25 pp. Avail. NTIS Order No. PAT-APPL-7-270 098. (Eng). CODEN: XAXXAV. APPLICATION: US 88-270098 14 Nov 1988.

AB Genes for parvovirus capsid proteins are expressed without export of

the proteins in transgenic CHO cells using the cognate promoter in an expression vector. Capsid proteins suitable for \*\*\*vaccination\*\*\* or prepn. of antisera for diagnosis are produced. The capsid proteins may also be usable for packaging and delivering DNA to a host system. The parvovirus capsid genes expressed from their own promoter were cloned into a vector using a dihydrofolate reductase gene driven by an SV40 promoter as a selectable marker. CHO cells were transformed with the construct and assayed for the prodn. of antigen and capsids. The cells produced cross-reacting material detectable by electron microscopy and they sedimented normally in sucrose gradients. Transformed cells grew normally.

L15 ANSWER 22 OF 27 COPYRIGHT 1992 ACS

CA108(9):70175h Recombinant parvovirus RA-1 products and its use for diagnosis of human connective tissue disorders. Simpson, Robert Wayne; Vanleeuwen, Donald Hugh; Smith, Robert Eldon; Lawrie, Dawson Keiss (Abbott Laboratories, USA). Eur. Pat. Appl. EP 238893 A2 30 Sep 1987, 21 pp. DESIGNATED STATES: R: BE, DE, FR, IT. (Eng). CODEN: EPXXDW. CLASS: ICM: C12N015-00. ICS: A61K039-23; C12Q001-70; G01N033-569. APPLICATION: EP 87-102923 2 Mar 1987. PRIORITY: US 86-841905 20 Mar 1986.

AB The single-stranded DNA of parvovirus RA-1 is isolated and its double-stranded synthetic DNA is cloned. The recombinant DNA products and the expressed gene products have utility as diagnostic reagents for the detn. of human connective tissue disorders. Recombinant plasmid pAPV3 contg. 5-95 map units of RA-1 virus genome was constructed. The DNA extd. from the synovial fluids of patients having rheumatoid arthritis hybridized efficiently to the DNA probe derived from pAPV3. The results correlates the presence of RA-1 virus in human tissues with human rheumatoid arthritis.

L15 ANSWER 23 OF 27 COPYRIGHT 1992 ACS

CA108(1):1510b Expression of \*\*\*human\*\*\* \*\*\*parvovirus\*\*\* \*\*\*B19\*\*\* structural protein in E. \*\*\*coli\*\*\* and detection of antiviral antibodies in human serum. Sisk, W. P.; Berman, M. L. (Bionetics Res., Inc., Rockville, MD 20850, USA). Bio/Technology, 5(10), 1077-80 (Eng) 1987. CODEN: BTCHDA. ISSN: 0733-222X.

AB \*\*\*Human\*\*\* \*\*\*parvovirus\*\*\* ( \*\*\*B19\*\*\* ), a small single stranded DNA virus, has been assocd. with a variety of different human diseases including aplastic crisis and erythema infectiosum. To date there is no practical source of viral antigen for screening potentially infected patients. Starting with previously isolated genomic clones and using a combination of in vitro and in vivo techniques, the major coding region of the B19 virion protein structural gene was expressed in Escherichia \*\*\*coli\*\*\* as a 196 kilodalton .beta.-galactosidase fusion protein. Using this recombinant antigen, antibodies to B19 from the sera of patients known to be infected with the virus were detected by Western blot anal. The sera from normal healthy individuals were also tested and 44% of the subjects showed a pos. immunoreaction to the B19-.beta.-galactosidase fusion protein.

L15 ANSWER 24 OF 27 COPYRIGHT 1992 ACS

CA107(25):230539q Characterization of adeno-associated virus rep proteins in human cells by antibodies raised against rep expressed in Escherichia \*\*\*coli\*\*\*. Trempe, James P.; Mendelson, Ella; Carter, Barrie J. (Lab. Mol. Cell. Biol., Natl. Inst. Diabetes and Dig. Kidney Dis., Bethesda, MD 20892, USA). Virology, 161(1), 18-28 (Eng) 1987. CODEN: VIRLAX. ISSN: 0042-6822.

AB The rep gene of the defective \*\*\*human\*\*\* \*\*\*parvovirus\*\*\*, adeno-assocd. virus (AAV), mediates several trans-acting functions important to virus replication, transcription, and gene expression. At least 4 overlapping polypeptides are expressed from the rep gene. A prokaryotic vector was constructed which expressed in E. \*\*\*coli\*\*\* a region of AAV comprising 93% of the largest AAV rep

protein. The protein expressed in E. **\*\*\*coli\*\*\***, rep78.93, was used to raise specific antibodies in rabbits. These antibodies were capable of detecting all 4 AAV rep proteins in human cells transfected with AAV-contg. plasmids as well as new species of 47 and 35 kDa mol. wt. These new rep proteins originate from the transcription promoter at map unit 19 in the AAV genome and may indicate use of alternate AUG codons or protein modification. The antibodies also recognized novel forms of the rep proteins expressed from mutant AAV genomes. Immunofluorescence anal. of AAV-infected human cells revealed that the rep proteins are localized primarily in the nucleus of the infected cell and have a distribution different from that of AAV capsid protein. These results demonstrate that antisera raised against an AAV rep protein synthesized in E. **\*\*\*coli\*\*\*** are capable of detecting wild-type AAV rep proteins in virus-infected mammalian cells. These specific antibodies should facilitate further characterization of the functionally pleiotropic viral rep proteins.

L15 ANSWER 25 OF 27 COPYRIGHT 1992 ACS

CA105(25):219894q Identification of the major structural and nonstructural proteins encoded by **\*\*\*human\*\*\*** **\*\*\*parvovirus\*\*\*** **\*\*\*B19\*\*\*** and mapping of their genes by prokaryotic expression of isolated genomic fragments. Cotmore, Susan F.; McKie, Virgil C.; Anderson, Larry J.; Astell, Caroline R.; Tattersall, Peter (Sch. Med., Yale Univ., New Haven, CT 06510, USA). ~~1. **Virion** 4:60(23), 548-57 (Eng) 1986.~~ CODEN: JOVIAM. ISSN: 0022-538X.

AB Plasma from a child with homozygous sickle-cell disease, sampled during the early phase of an aplastic crisis, contained **\*\*\*human\*\*\*** **\*\*\*parvovirus\*\*\*** **\*\*\*B19\*\*\*** virions. Plasma taken 10 days later (during the convalescent phase) contained both IgM and IgG antibodies directed against 2 viral polypeptides with apparent mol. wts. of 83,000 and 58,000 which were present exclusively in the particulate fraction of the plasma taken during the acute phase. These 2 protein species comigrated at 110 S on neutral sucrose velocity gradients with the B19 viral DNA and, thus, appear to constitute the viral capsid polypeptides. The B19 genome was mol. cloned into a bacterial plasmid vector. Restriction endonuclease fragments of this cloned B19 genome were treated with BAL 31 and shotgun cloned into the open reading frame expression vector pJS413. Two expression constructs contg. B19 sequences from different halves of the viral genome were obtained, which directed the synthesis, in bacteria, of segments of virally encoded protein. These polypeptide fragments were then purified and used to **\*\*\*immunize\*\*\*** rabbits. Antibodies against a protein sequence specified between nucleotides 2897 and 3749 recognized both the 83- and 58-kilodalton capsid polypeptides in aplastic plasma taken during the acute phase and detected similar proteins in the tissues of a stillborn fetus which had been infected transplacentally with B19. Antibodies against a protein sequence encoded in the other half of the B19 genome (nucleotides 1072-2044) did not react specifically with any protein in plasma taken during the acute phase but recognized 3 nonstructural polypeptides of 71, 63, and 52 kilodaltons present in the liver and, at lower levels, in some other tissues of the transplacentally infected fetus.

L15 ANSWER 26 OF 27 COPYRIGHT 1992 ACS

CA100(21):169358s Molecular cloning of adeno-associated virus variant genomes and generation of infectious virus by recombination in mammalian cells. Senapathy, Periannan; Carter, Barrie J. (Lab. Cell Biol. Genet., Natl. Inst. Arthritis, Diab. Dig. Kidney Dis., Bethesda, MD 20205, USA). J. Biol. Chem., 259(7), 4661-6 (Eng) 1984. CODEN: JBCHA3. ISSN: 0021-9258.

AB Continued passage of the **\*\*\*human\*\*\*** **\*\*\*parvovirus\*\*\*** adeno-assocd. virus (AAV), at high multiplicity of infection in human cells results in the accumulation of AAV particles contg. variant genomes. The structure of individual variant AAV genomes was

analyzed by mol. cloning in the Escherichia \*\*\*coli\*\*\* plasmid, pBR328. Each of the AAV inserts in 6 individual, recombinant plasmids contained a single internal deletion, but in contrast to a previous model, the locations of the deletions were nonrandom. The mol. cloning protocol also generated recombinant plasmids contg. the entire AAV2 DNA sequence which yielded infectious AAV particles when transfected into human 293 cells in the presence of helper adenovirus using a DEAE-transfection procedure. Infectious AAV genomes were also generated by recombination when cells were jointly transfected with a mixt. of plasmids contg. 2 different mutant AAV genomes. The efficiency of this recombination appeared to be influenced by the degree of homol. between the mutant AAV genomes.

L15 ANSWER 27 OF 27 COPYRIGHT 1992 ACS

CA99(15):117134g Cloning of infectious adeno-associated virus genomes in bacterial plasmids. Laughlin, Catherine A.; Tratschin, Jon Duri; Coon, Helen; Carter, Barrie J. (Lab. Cell Biol. Genet., NIADDK, Bethesda, MD 20205, USA). Gene, 23(1), 65-73 (Eng) 1983. CODEN: GENED6. ISSN: 0378-1119.

AB The construction of 2 Escherichia \*\*\*coli\*\*\* hybrid plasmids, each of which contains the entire 4.7-kilobase DNA genome of the \*\*\*human\*\*\* \*\*\*parvovirus\*\*\*, adeno-assocd. virus (AAV) type 2, is described. Since the AAV genome was inserted into the plasmid DNA with BglII linkers, the entire virus genome can be recovered by in vitro cleavage of the purified recombinant plasmid. Transfection of these recombinant DNAs into an adenovirus-transformed human cell line in the presence of helper adenovirus resulted in efficient rescue and replication of the AAV genome and prodn. of fully infectious virus particles. These AAV-plasmid recombinant DNA mols. should be useful both for site-specific mutagenesis of the viral genome and to study the potential of AAV as a eukaryotic vector.

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L19 ANSWER 1 OF 23 COPYRIGHT 1992 ACS

CA117(15):144526h Regulated high level expression of a human .gamma.-globin gene introduced into erythroid cells by an adeno-associated virus \*\*\*vector\*\*\*. Walsh, Christopher E.; Liu, Johnson M.; Xiao, X.; Young, Neal S.; Nienhuis, Arthur W.; Samulski, Richard Jude (Clin. Hematol. Branch, Natl. Heart Lung and Blood Inst., Bethesda, MD 20892, USA). Proc. Natl. Acad. Sci. U. S. A., 89(15), 7257-61 (Eng) 1992. CODEN: PNASA6. ISSN: 0027-8424.

AB Gene therapy of severe hemoglobinopathies will require high-level expression of a transferred globin gene in erythroid cells. Distant regulatory elements flanking the .beta.-globin gene cluster, the locus control region, are needed for appropriate expression. The use of a \*\*\*human\*\*\* \*\*\*parvovirus\*\*\*, the adeno-assocd. virus (AAV), for globin gene transfer is explored here. The human A.gamma.-globin gene, linked to hypersensitivity site 2 from the locus control region of the .beta.-globin gene cluster, was subcloned into a plasmid (psub201) contg. the AAV inverted terminal repeats. This construct was cotransfected with a helper plasmid contg. trans-acting AAV genes into human 293 cells that had been infected with adenovirus. The recombinant AAV \*\*\*vector\*\*\* contg. hypersensitivity site 2 stably introduced on av. one or two unrearranged proviral copies into human K562 erythroleukemia cells. The transferred globin gene exhibited normal regulation upon hemin induction of erythroid maturation and was expressed at a level equiv. to a native chromosomal A.gamma.-globin gene.

L19 ANSWER 2 OF 23 COPYRIGHT 1992 ACS

CA117(13):125860w A block in full-length transcript maturation in cells nonpermissive for \*\*\*B19\*\*\* \*\*\*parvovirus\*\*\*. Liu, Johnson M.; Green, Spencer W.; Shimada, Takashi; Young, Neal S. (Clin.

- AB Vertebrate parvoviruses share a similar genomic organization, with the capsid proteins encoded by genes on the right side and nonstructural proteins encoded by genes on the left side. The temporal and cell-specific appearances of these 2 types of gene products are regulated by a variety of genetic mechanisms. Rodent parvovirus structural proteins, for example, are encoded by a sep. promoter which is pos. regulated by nonstructural-gene products. In contrast, for the human \*\*\*B19\*\*\* \*\*\*parvovirus\*\*\*, the analogous structural-gene promoter is nonfunctional, and both left- and right-side transcripts originate from a single promoter and are highly processed. A combination of sensitive RNA analyses of wild-type and mutant templates was to show that the relative abundance of these alternatively processed transcripts appears to be governed by unique postinitiation events. In permissive cells, the steady-state level of right-side structural-gene transcripts predominates over that of left-side nonstructural-gene transcripts. In nonpermissive cells transfected with the B19 virus genome, nonstructural-gene transcripts predominate. Removal of 3' processing signals located in the middle of the viral genome increases transcription of the far right side. Disruption of a polyadenylation signal in this region makes readthrough of full-length right-side transcripts possible. These results suggest that the abundance of B19 virus RNAs is detd. by active 3' processing and is coupled to DNA template replication.

L19 ANSWER 3 OF 23 COPYRIGHT 1992 ACS

CA116(1):4770n Peptides from \*\*\*human\*\*\* \*\*\*parvovirus\*\*\*  
\*\*\*B19\*\*\* . Fridell, Eva; Blinkovski, Alexander; Mannervik, Mattias; Ruden, Ulla; Wahren, Britta; Trojnar, Jerzy (Dep. Virol., Natl. Bacteriol. Lab., Stockholm S-105 21, Swed.). Pept. 1990, Proc. Eur. Pept. Symp., 21st, Meeting Date 1990, 905-7. Edited by: Giralt, Ernest; Andreu, David. ESCOM Sci. Publ.: Leiden, Neth. (Eng) 1991. CODEN: 57HNAI.

- AB Three short linear antigenic regions were identified in the structural proteins of \*\*\*B19\*\*\* \*\*\*parvovirus\*\*\*. Two of them derive from a region representing \*\*\*VP1\*\*\* and the 3rd from a part which may represent either \*\*\*VP1\*\*\* or \*\*\*VP2\*\*\*. B19-infected persons react with these regions with specific IgG and/or IgM in varying proportions. The region in \*\*\*VP1\*\*\* - \*\*\*VP2\*\*\* is also immunogenic and gives a high titer of specific antibodies in rabbits.

L19 ANSWER 4 OF 23 COPYRIGHT 1992 ACS

CA115(25):277379t Identification and mapping of neutralizing epitopes of \*\*\*human\*\*\* \*\*\*parvovirus\*\*\* \*\*\*B19\*\*\* by using human antibodies. Sato, Hiroyuki; Hirata, Jouji; Kuroda, Naotaka; Shiraki, Hiroshi; Maeda, Yoshiaki; Okochi, Kazuo (Clin. Lab., Kyushu Univ. Hosp., Fukuoka 812, Japan). J. Virol., 65(10), 5485-90 (Eng) 1991. CODEN: JOVIAM. ISSN: 0022-538X.

- AB The regions responsible for neutralization in the \*\*\*human\*\*\* \*\*\*parvovirus\*\*\* \*\*\*B19\*\*\* -structural protein were identified and mapped by using region-specific human antibodies derived from seropos. blood donors. The region-specific antibodies were purified by using affinity columns coupled with synthetic peptides of the hydrophilic regions including the :beta.-turn structure deduced by the predicted secondary structure of \*\*\*VP2\*\*\*. Fifteen highly specific antibodies against the synthetic peptides were obtained. Ten of them were able to ppt. the radiolabeled virus. Six of them proved to be able to protect the colony-forming unit erythroid cells in human bone marrow cell cultures from injury by the virus. The sequences recognized by the 6 neutralizing antibodies were sites corresponding to amino acids 253-272, 309-330, 325-346, 359-382, 449-468 and 491-515 from the N-terminal portion of \*\*\*VP2\*\*\*.

These observations suggest that the neutralizing epitopes were distributed in the region from amino acid 253 in the N-terminal portion of \*\*\*VP2\*\*\* to the C terminus of \*\*\*VP2\*\*\*.

L19 ANSWER 5 OF 23 COPYRIGHT 1992 ACS

CA115(25):277240r The use of labeled fusion protein for detection of \*\*\*B19\*\*\* \*\*\*parvovirus\*\*\* IgM antibodies by an immunocapture test. Morinet, F.; Courouce, A. M.; Galibert, F.; Perol, Y. (Serv. Bacteriol.-Virol., Hop. Saint-Louis, Paris 75010, Fr.). J. Virol. Methods, 32(1), 21-30 (Eng) 1991. CODEN: JYMEDH. ISSN: 0166-0934.

AB A new anti-B19 IgM ELISA was developed taking advantage of antibody-capture with biotinylated fusion protein as antigen. Specificity was examd. using serum IgM antibody pos. for rubella, hepatitis B core antigen, cytomegalovirus and Epstein-Barr virus as well as with sera pos. for rheumatoid factors or antinuclear antibodies. The specificity was 96%. Of one hundred serum samples compared using the new ELISA or the std. MACRIA tests for the presence of B19 IgM, 88 gave the same results. Fifty-three were neg. and 35 were pos. Six sera were ELISA-neg. MACRIA-pos., and six MACRIA-neg. ELISA-pos. Thus, the ELISA gave 90% agreement with MACRIA. In a clin. study with 725 sera from suspected B19 infections, 161 (22%) were found pos. by ELISA. The pos. sera were from patients suffering from arthritis (35%), rash (35%), acute or chronic erythroblastopenia (21%), pancytopenia (5%), vascular purpura (2%) and lymphadenopathy (2%). A series of serum specimens obtained from two-B19 infected individuals were also studied. The IgM antibody became undetectable after four months.

L19 ANSWER 6 OF 23 COPYRIGHT 1992 ACS

CA115(21):224957y Genetic diversity of \*\*\*human\*\*\* \*\*\*parvovirus\*\*\* \*\*\*B19\*\*\* determined using a set of restriction endonucleases recognizing four or five base pairs and partial nucleotide sequencing: use of sequence variability in virus classification. Umene, Kenichi; Nunoue, Tadasu (Fac. Med., Kyushu Univ., Fukuoka 812, Japan). J. Gen. Virol., 72(8), 1997-2001 (Eng) 1991. CODEN: JGVIAY. ISSN: 0022-1317.

AB Anal. of the restriction site polymorphism (RSP) of \*\*\*human\*\*\* \*\*\*parvovirus\*\*\* \*\*\*B19\*\*\* using 12 restriction endonucleases (REs) recognizing 4 or 5 bp sequences (4- or 5-bp REs) revealed a significant difference between strains previously classified as being of the same genome type, and a relationship between 2 strains of different genome types, thereby indicating a global spread of B19 virus strains. These findings demonstrate the advantage of this set of 4- and 5-bp REs for the calcn. of the degree of genetic diversity and clearly it is necessary to amend the taxonomy of B19 virus strains using these REs. The nucleotide (nt) sequence was examd. between nt 3141 and 3411, at the N terminus of the \*\*\*VP2\*\*\* protein coding region, in 12 B19 virus strains. The pattern of distribution of nucleotide differences between the strains confirmed the classification by RSP anal. Between nt 3293 and nt 3364, a region in which an antigenic epitope may be encoded, there was no evidence of a nucleotide change causing an amino acid change. Thus, the amino acid sequence in this potential epitope is probably conserved.

L19 ANSWER 7 OF 23 COPYRIGHT 1992 ACS

CA115(15):156527f Evaluation of a synthetic-peptide enzyme-linked immunosorbent assay for immunoglobulin M to \*\*\*human\*\*\* \*\*\*parvovirus\*\*\* \*\*\*B19\*\*\*. Fridell, E.; Cohen, B., J.; Wahren, B. (Dep. Virol., Karolinska Inst., Stockholm S-105 21, Swed.). J. Clin. Microbiol., 29(7), 1376-81 (Eng) 1991. CODEN: JCMIDW. ISSN: 0095-1137.

AB A synthetic peptide corresponding to a part of the virus protein 1-virus protein 2 overlapping region of \*\*\*human\*\*\* \*\*\*parvovirus\*\*\* \*\*\*B19\*\*\* was used in an indirect ELISA. Antibodies of the IgM class were measured in serum samples from

patients with erythema infectiosum and controls. In comparison with an IgM assay using native B19 viral antigen, the peptide assay was 92% sensitive and 87% specific. B19 IgM reactivities were seen in a limited no. of children with other viral diseases. Specific IgM reactivities to short synthetic viral peptides have previously been reported only with Epstein-Barr virus. Since other sources of viral antigen are limited, the peptide antigen assay may be a useful alternative for the diagnosis of B19-assocd. disease in human beings.

L19 ANSWER 8 OF 23 COPYRIGHT 1992 ACS

CA115(7):69649d A cyclized peptide for studies of \*\*\*human\*\*\*  
\*\*\*parvovirus\*\*\* \*\*\*B19\*\*\* infection. Fridell, Eva; Trojnar, Jerzy; Mehlin, Hans; Wahren, Britta (Dep. Virol., Natl. Bacteriol. Lab., Stockholm S-105 21, Swed.). J. Immunol. Methods, 138(1), 125-8 (Eng) 1991. CODEN: JIMMBG. ISSN: 0022-1759.

AB Synthetic peptides corresponding to \*\*\*human\*\*\*  
\*\*\*parvovirus\*\*\* \*\*\*B19\*\*\* sequences were evaluated for immunoreactivity with the sera of infected persons. A cyclized peptide deduced from the N terminus of viral protein \*\*\*VP2\*\*\* and contg. the amino acids 284-307 showed a high reactivity with IgM class antibodies when comparing seropos. and seroneg. sera.

L19 ANSWER 9 OF 23 COPYRIGHT 1992 ACS

CA115(5):42918d Analysis of splice junctions and in vitro and in vivo translation potential of the small, abundant \*\*\*B19\*\*\*  
\*\*\*parvovirus\*\*\* RNAs. St. Amand, Jan; Beard, Caroline; Humphries, Keith; Astell, Caroline R. (Dep. Biochem., Univ. British Columbia, Vancouver, BC V6T 1W5, Can.). Virology, 183(1), 133-42 (Eng) 1991. CODEN: VIRLAX. ISSN: 0042-6822.

AB Two \*\*\*parvovirus\*\*\* \*\*\*B19\*\*\* cDNA libraries have been constructed, 1 from COS-7 cells transfected with a B19/pSV0d hybrid \*\*\*vector\*\*\* and the other from B19-infected human erythroid leukemic cells. These libraries were used to investigate the expression of the abundant classes of polyadenylated B19 RNAs; the 700- and 800-nt class which terminates in the middle of the genome and the 500- and 600-nt class which contains an ORF from the extreme right-hand end of the genome. The 700- and 800-nt RNA species were not found in the COS cell library, suggesting that a variant polyadenylation signal (ATTAAA or AATAAC) in the middle of the genome is not efficiently recognized in these cells. In contrast, the 700- and 800-nt class was highly represented in the human library, confirming the use of this variant polyadenylation signal in the normal host cell of the virus. In COS cells the middle exon of the 500- and 600-nt class of RNA exhibited variability in both splice donor and acceptor sites. However, in human cells there were only 2 splice acceptor sites nt 1910 and 2030, and a single splice donor site nt 2183 for this exon. Antisera, prepd. against a peptide derived from the 94-aa potential protein encoded by the 500- and 600-nt class of RNA, recognized, on a Western blot, a polypeptide of approx. 11 kDa that was translated in vitro from these cDNAs and in vivo in pSV0d/B19 transfected COS cells. Immunopptn. revealed that 2 proteins were made from this ORF, suggesting the use of internal translation initiation site(s). Another antisera, raised against a second peptide corresponding to an antigenic region of the potential protein encoded by the 700- and 800-nt class of RNA, failed to detect a 15-kDa protein by Western blotting or immunopptn. of labeled proteins both in vitro and in vivo in COS cells.

L19 ANSWER 10 OF 23 COPYRIGHT 1992 ACS

CA114(25):245579w Identification of the region including the epitope for a monoclonal antibody which can neutralize \*\*\*human\*\*\*  
\*\*\*parvovirus\*\*\* \*\*\*B19\*\*\*. Sato, Hiroyuki; Hirata, Jouji; Furukawa, Michiyo; Kuroda, Naotaka; Shiraki, Hiroshi; Maeda, Yoshiaki; Okochi, Kazuo (Clin. Lab., Kyushu Univ. Hosp., Fukuoka 812, Japan). J. Virol., 65(4), 1667-72 (Eng) 1991. CODEN: JOVIAM.

AB The authors identified a region in the \*\*\*human\*\*\*  
 \*\*\*parvovirus\*\*\* structural protein involved in neutralization of  
 the virus by a monoclonal antibody. A newly established monoclonal  
 antibody reacted with both viral capsid proteins \*\*\*VP1\*\*\* and  
 \*\*\*VP2\*\*\*. The epitope was found in six strains of independently  
 isolated \*\*\*human\*\*\* \*\*\*parvovirus\*\*\* \*\*\*B19\*\*\*. The  
 monoclonal antibody could protect erythroid colony-forming units in  
 human bone marrow cell culture from injury by the virus. The  
 monoclonal antibody reacted with only 1 of 12 peptides that were  
 synthesized according to a predicted amino acid sequence based on  
 nucleotide sequences of the coding region for the structural protein  
 of B19 virus. The sequence recognized by the antibody was a site  
 corresponding to amino acids 328 to 344 from the N-terminal portion  
 of \*\*\*VP2\*\*\*. This evidence suggests that the epitope of the  
 viral capsid protein is located on the surface of the virus and may  
 be recognized by virus-neutralizing antibodies.

L19 ANSWER 11 OF 23 COPYRIGHT 1992 ACS

CA114(15):141049g New oligopeptide immunoglobulin G test for  
 \*\*\*human\*\*\* \*\*\*parvovirus\*\*\* \*\*\*B19\*\*\* antibodies.  
 Schwarz, Tino F.; Modrow, Susanne; Hottentraeger, Barbara;  
 Hoeflacher, Brigitte; Jaeger, Gundula; Scharlt, Wolfgang; Sumazaki,  
 Ryo; Wolf, Hans; Middeldorp, Jaap; et al. (Max von Pettenkofer Inst.  
 Hyg. Med. Microbiol., Ludwig-Maximilians-Univ., Munich 8000/2, Fed.  
 Rep. Ger.). J. Clin. Microbiol., 29(3), 431-5 (Eng) 1991. CODEN:  
 JCMIDW. ISSN: 0095-1137.

AB A new, highly sensitive and specific enzyme immunoassay using  
 oligopeptides as antigen (ELISA B19-OP) for detecting  
 \*\*\*parvovirus\*\*\* \*\*\*B19\*\*\* -specific IgG was established. As  
 antigens, B19-specific oligopeptides of 24 and 30 kDa derived from a  
 196-kDa fusion protein of .beta.-galactosidase and viral capsid  
 protein ( \*\*\*VP1\*\*\* ) of B19 after CNBr cleavage and sepn. by HPLC  
 were used. Of 139 serum specimens tested in parallel for anti-B19  
 IgG by std. ELISA using B19 particles as antigen and by ELISA  
 B19-OP, 73 (52.5%) were pos. and 63 (45.3%) were neg. in both tests,  
 and 3 (2.2%) were neg. by std. ELISA but pos. by ELISA B19-OP and by  
 immunoblot. By using ELISA B19-OP, it was possible to detect  
 anti-B19 IgG in an asymptomatic blood donor 4 wk after acute  
 infection, and anti-B19 IgG titers of 10<sup>-5</sup> could be measured in  
 convalescent-phase sera.

L19 ANSWER 12 OF 23 COPYRIGHT 1992 ACS

CA113(13):113899v Propagation of \*\*\*human\*\*\* \*\*\*parvovirus\*\*\*  
 with erythroblast of fetus liver. Sugawara, Kazuo (Mitsubishi Kasei  
 Corp., Japan). Jpn. Kokai Tokkyo Koho JP 02092279 A2 3 Apr 1990  
 Heisei, 6 pp. (Japan). CODEN: JKXXAF. CLASS: ICM: C12N007-00.  
 ICS: A61K039-23. ICI: C12N007-00, C12R001-91. APPLICATION: JP  
 88-242166 27 Sep 1988.

AB Tumor parvovirus is propagated in vitro by first adsorbing the virus  
 on the erythroblasts of human fetal liver and then culturing the  
 erythroblast. The method can be used in prepg. the viral antigen and  
 antibody for diagnosis. Erythroblast cells obtained from an abortive  
 fetus liver was incubated with human parovovirus for 2 h at  
 4.degree. for adsorption. After repeated washing, the virus-adsorbed  
 erythroblast cells was given cultured for 37.degree. under 5% CO2  
 for 15 days. The propagation of parvovirus by expression of the  
 viral structure protein \*\*\*VP\*\*\* - \*\*\*1\*\*\* and \*\*\*VP\*\*\* -  
 \*\*\*2\*\*\*, detd. by western blotting.

L19 ANSWER.13 OF 23 COPYRIGHT 1992 ACS

CA112(13):115051r Detection of \*\*\*human\*\*\* \*\*\*parvovirus\*\*\*  
 \*\*\*B19\*\*\* DNA by using the polymerase chain reaction. Koch,  
 William C.; Adler, Stuart P. (Child. Med. Cent., Med. Coll.  
 Virginia, Richmond, VA 23298, USA). J. Clin. Microbiol., 28(1),  
 65-9 (Eng) 1990. CODEN: JCMIDW. ISSN: 0095-1137.



AB The polymerase chain reaction (PCR) was investigated for detecting  
\*\*\*human\*\*\* \*\*\*parvovirus\*\*\* \*\*\*B19\*\*\* (B19) DNA in sera.  
Three pairs of oligonucleotides were evaluated as primers. The best  
oligonucleotide pair spanned 699 nucleotides, including the region  
common to \*\*\*VP1\*\*\* and \*\*\*VP2\*\*\*. After PCR amplification  
of B19 DNA in serum, a 699-nucleotide DNA fragment was detected on  
agarose gels. This DNA fragment was B19 DNA, because after Southern  
transfer it hybridized to a 19-nucleotide internal probe and  
contained a single PstI cleavage site. Dot blot hybridization with a  
radiolabeled cloned portion of the B19 genome as a probe was  
compared with PCR. PCR was 104 times more sensitive than dot blot  
hybridization and, with an internal radiolabeled probe, 107 times  
more sensitive than dot blot hybridization. Of 29 serum specimens  
from 18 patients with proven B19 infections, 24 were PCR pos. None  
of 20 serum samples from uninfected controls were pos. Of 22 serum  
samples pos. for IgM to B19, PCR detected B19 DNA in 17. Seven serum  
samples lacking IgM were PCR pos. PCR detected B19 DNA in urine,  
amniotic fluid, pleural fluid, ascites, and leukocyte exts. PCR is a  
rapid and simple method for diagnosing infections with \*\*\*human\*\*\*  
\*\*\*parvovirus\*\*\* \*\*\*B19\*\*\* but must be combined with serol.  
tests for IgM to B19, esp. when testing only a single serum sample.

L19 ANSWER 14 OF 23 COPYRIGHT 1992 ACS

CA111(25):226172e Construction of a recombinant \*\*\*human\*\*\*  
\*\*\*parvovirus\*\*\* \*\*\*B19\*\*\* : adeno-associated virus 2 (AAV)  
DNA inverted terminal repeats are functional in an AAV-B19 hybrid  
virus. Srivastava, Carolyn H.; Samulski, Richard J.; Lu, Li;  
Larsen, Steven H.; Srivastava, Arun (Sch. Med., Indiana Univ.,  
Indianapolis, IN 46202, USA). Proc. Natl. Acad. Sci. U. S. A.,  
86(20), 8078-82 (Eng) 1989. CODEN: PNASA6. ISSN: 0027-8424.

AB To facilitate genetic anal. of the human pathogenic parvovirus B18,  
a hybrid B19 viral genome was constructed in which the defective B19  
inverted terminal repeats were replaced with the full-length  
inverted terminal repeats from a nonpathogenic \*\*\*human\*\*\*  
\*\*\*parvovirus\*\*\*, the adeno-assocd. virus 2 (AAV). The hybrid  
AAV-B19 genome was rescued from a recombinant plasmid and then the  
DNA was replicated upon transfection into adenovirus 2-infected  
human KB cells in the presence of AAV genes coding for proteins  
required for AAV DNA replication (AAV-Rep proteins). In addn., in  
the presence of AAV genes coding for the viral capsid proteins  
(AAV-Cap proteins), the rescued/replicated hybrid AAV-B19 genomes  
were packaged into mature AAV progeny virions, which were  
subsequently released into culture supernatants. The recombinant  
AAV-B19 progeny virions were infectious for normal human bone marrow  
cells and strongly suppressed erythropoiesis in vitro. The  
availability of an infectious recombinant B19 virus should  
facilitate the mutational anal. of the viral genome, which, in turn,  
may yield information on individual viral gene functions in  
B19-induced pathogenesis. The hybrid AAV-B19 genome may also prove  
to be a useful \*\*\*vector\*\*\* for gene transfer in human bone  
marrow cells.

L19 ANSWER 15 OF 23 COPYRIGHT 1992 ACS

CA111(23):209796u Transient expression of \*\*\*B19\*\*\*  
\*\*\*parvovirus\*\*\* gene products in COS-7 cells transfected with  
B19-SV40 hybrid \*\*\*vectors\*\*\*. Beard, Caroline; St. Amand,  
Janet; Astell, Caroline R. (Fac. Med., Univ. British Columbia,  
Vancouver, BC V6T 1W5, Can.). Virology, 172(2), 659-64 (Eng) 1989.  
CODEN: VIRLAX. ISSN: 0042-6822.

AB Hybrid \*\*\*B19\*\*\* \*\*\*parvovirus\*\*\* -SV40 origin  
\*\*\*vectors\*\*\* were transfected into COS-7 cells and replication of  
these plasmids studied. Plasmids that have a frameshift mutation  
within the nonstructural gene region replicated to high level (copy  
no. .apprx.10,000/transfected cell) although somewhat lower than  
pSV0d, the SV40 origin \*\*\*vector\*\*\* without B19 sequence (copy  
no. .apprx.100,000/transfected cell). However, hybrid \*\*\*B19\*\*\*

\*\*\*parvovirus\*\*\* -SV40 origin \*\*\*vectors\*\*\* that do not contain these frameshift mutations replicated to a much lower level (copy no. .apprx.1000/transfected cell). Although the hybrid \*\*\*vectors\*\*\* studied replicated at different efficiencies in COS-7 cells, they are transcribed at approx. the same level, resulting in RNA species that are indistinguishable from those seen in B19 virus-infected erythroid bone marrow cells. Western blot anal. demonstrated that the mRNAs are translated into polypeptides of the same size and, in the case of viral structural proteins, the same relative abundance as seen in a B19-infected clin. sample.

L19 ANSWER 16 OF 23 COPYRIGHT 1992 ACS

CA111(7):53998y Replication of a \*\*\*human\*\*\* \*\*\*parvovirus\*\*\* nonsense mutant in mammalian cells containing an inducible amber suppressor. Chejanovsky, Nor; Carter, Barrie J. (Lab. Mole. Cell. Biol., Natl. Inst. Diabetes Dig. Kidney Dis., Bethesda, MD 20892, USA). Virology, 171(1), 239-47 (Eng) 1989. CODEN: VIRLAX. ISSN: 0042-6822.

AB When recombinant plasmids contg. the entire adeno-assocd. virus (AAV) genome are transfected into permissive cells infected with a helper adenovirus, infectious AAV particles are efficiently generated. These plasmids can be used to generate mutant AAV genomes or recombinant AAV \*\*\*vectors\*\*\*. Packaging of mutant AAV genomes has required complementation with a second AAV plasmid in the transfection assay which may lead to generation of significant amts. of wild-type AAV recombinants. One approach to alleviate this problem was to generate conditional lethal mutants. An AAV plasmid recombinant having a nonsense mutation in the AAV rep gene was constructed by using oligonucleotide-directed mutagenesis to convert a serine codon to an amber codon. This mutant AAV can be grown on monkey cell lines contg. an inducible human serine tRNA amber suppressor. The amber suppression is quite efficient and yields a burst of mutant AAV particles at about 10% of the titer of wild-type AAV. The reversion frequency of the amber mutation appears to be <10<sup>-5</sup>.

L19 ANSWER 17 OF 23 COPYRIGHT 1992 ACS

CA111(3):20692r Molecular study of the B19 (human) pathogenic parvovirus. Ayub, Jamshed (Old Dominion Univ., Norfolk, VA, USA). 112 pp. Avail. Univ. Microfilms Int., Order No. DA8823948 From: Diss. Abstr. Int. B 1989, 49(8), 3156 (Eng) 1988.

AB Unavailable

L19 ANSWER 18 OF 23 COPYRIGHT 1992 ACS

CA109(17):143557s Translational regulation of \*\*\*B19\*\*\* \*\*\*parvovirus\*\*\* capsid protein production by multiple upstream AUG triplets. Ozawa, Keiya; Ayub, Jamshed; Young, Neal (Cell Biol. Sect., Natl. Heart, Lung Blood Inst., Bethesda, MD 20892, USA). J. Biol. Chem., 263(22), 10922-6 (Eng) 1988. CODEN: JBCHA3. ISSN: 0021-9258.

AB The \*\*\*B19\*\*\* \*\*\*parvovirus\*\*\* produces 2 capsid proteins in strikingly different quantities ( \*\*\*VP1\*\*\* < 4%, \*\*\*VP2\*\*\* > 96%) from overlapping RNAs that are derived from the same transcription unit. Immediately upstream from the \*\*\*VP1\*\*\* translation initiation site is an unusual sequence contg. multiple ATG triplets. During RNA processing, this sequence is spliced out of \*\*\*VP2\*\*\* RNA. To test the regulatory role of this sequence contg. upstream AUGs in translation, synthetic RNAs were produced in vitro by T7 RNA polymerase from various plasmid constructions. Translation of \*\*\*VP1\*\*\* RNA was very inefficient compared to \*\*\*VP2\*\*\* RNA in a cell-free system, indicating that capsid protein prodn. was regulated at the level of translation. Removal of upstream AUG sequences from \*\*\*VP1\*\*\* RNA greatly increased the efficiency of translation. Conversely, the addn. of the same AUG-rich sequence upstream of the initiation site of \*\*\*VP2\*\*\* decreased its translation. Thus, an upstream AUG-rich region acts as a neg.

regulatory element in the translational control of B19 capsid protein prodn.

L19 ANSWER 19 OF 23 COPYRIGHT 1992 ACS

CA105(17):147214t Negative and positive regulation in trans of gene expression from adeno-associated virus \*\*\*vectors\*\*\* in mammalian cells by a viral rep gene product. Tratschin, Jon Duri; Tal, Jacov; Carter, Barrie J. (Lab. Mol. Cellul. Biol., Natl. Inst. Arthritis, Diabet., Digest. Kidney Dis., Bethesda, MD 20892, USA). Mol. Cell. Biol., 6(8), 2884-94 (Eng) 1986. CODEN: MCEBD4. ISSN: 0270-7306.

AB The \*\*\*human\*\*\* \*\*\*parvovirus\*\*\*, adeno-assocd. virus (AAV), has been used as a \*\*\*vector\*\*\* for transient expression in mammalian cells of the gene for chloramphenicol acetyltransferase (CAT). In the AAV \*\*\*vector\*\*\*, pTS1, the CAT gene is expressed under the control of the major AAV promoter p40. This promoter is embedded within the carboxyl-terminal region of an open reading frame (orf-1) which codes for a protein (rep) required for AAV DNA replication. The rep product has addnl. trans-acting properties to regulate gene expression. First, deletion or frame-shift mutations in orf-1, which occurred far upstream of p40, increased expression of CAT in human 293 (adenovirus-transformed) cells. This increased CAT expression was abolished when such mutant AAV \*\*\*vectors\*\*\* were transfected into 293 cells together with a 2nd AAV \*\*\*vector\*\*\* which could supply the wild-type AAV rep product in trans. Thus, an AAV rep gene product was a neg. regulator, in trans, of expression of CAT in uninfected 293 cells. In adenovirus-infected 293 cells, the function of the AAV rep product was more complex, but in some cases, it appeared to be a trans activator of the expression from p40. In HeLa cells, only trans activation by rep was seen in the absence or presence of adenovirus. Neither activation nor repression by the rep product required replication per se of the AAV \*\*\*vector\*\*\* DNA. Thus, trans-acting neg. or pos. regulation of gene expression by the AAV rep gene is modulated by factors in the host cell and by the helper adenovirus.

L19 ANSWER 20 OF 23 COPYRIGHT 1992 ACS

CA105(7):55398c Nucleotide sequence and genome organization of \*\*\*human\*\*\* \*\*\*parvovirus\*\*\* \*\*\*B19\*\*\* isolated from the serum of a child during aplastic crisis. Shade, Rosemary O.; Blundell, Matthew C.; Cotmore, Susan F.; Tattersall, Peter; Astell, Caroline R. (Fac. Med., Univ. British Columbia, Vancouver, BC V6T 1W5, Can.). J. Virol., 58(3), 921-36 (Eng) 1986. CODEN: JOVIAM. ISSN: 0022-538X.

AB The nucleotide sequence of an almost-full-length clone of \*\*\*human\*\*\* \*\*\*parvovirus\*\*\* \*\*\*B19\*\*\* was detd. Whereas the extreme left and right ends of this genomic clone are incomplete, the sequence clearly indicates that the 2 ends of viral DNA are related by inverted terminal repeats similar to those of the Dependovirus genes. The coding regions are complete in the cloned DNA, and the 2 large open reading frames which span almost the entire genome are restricted to 1 strand, as has been found for all other parvoviruses characterized to date. From the DNA sequence it is concluded that the organization of the B19 transcription units is similar, although not identical, to those of other parvoviruses. In particular, the B19 genome may utilize a 4th promoter to transcribe mRNA encoding the major structural polypeptide, \*\*\*VP2\*\*\*. Anal. of the putative polypeptides confirms that B19 is only distantly related to the other parvoviruses but reveals that there is a small region in the gene probably encoding the major nonstructural protein of B19 that is closely conserved between all of the parvovirus genomes for which sequence information is currently available.

L19 ANSWER 21 OF 23 COPYRIGHT 1992 ACS

CA102(5):40939u Characterization and molecular cloning of a \*\*\*human\*\*\* \*\*\*parvovirus\*\*\* genome. Cotmore, Susan F.;

Tattersall, Peter (Sch. Med., Yale Univ., New Haven, CT 06510, USA).  
Science (Washington, D. C., 1983-), 226(4679), 1161-5 (Eng) 1984.  
CODEN: SCIEAS. ISSN: 0036-8075.

AB The genome of the small human virus serol. assocd. with erythrocyte  
aplasia and erythema infectiosum (fifth disease) is shown to be a  
linear, nonpermuted, single-stranded DNA mol. with self-priming  
hairpin termini, properties which are characteristic of the genomes  
of the family Parvoviridae. This \*\*\*human\*\*\* \*\*\*parvovirus\*\*\*  
chromosome was molecularly cloned into bacterial plasmid  
\*\*\*vectors\*\*\*, and the cloned DNA was used to explore its  
relatedness to other mammalian parvovirus serotypes by DNA:DNA  
hybridization. It is not related to the human adeno-assocd. viruses  
but does show a distant evolutionary relationship to genomes of the  
helper-independent parvoviruses of rodents. This strongly suggests  
that it is an autonomous parvovirus and, as such, is the 1st example  
of a member of this group of common animal pathogens to cause  
disease in man.

L19 ANSWER 22 OF 23 COPYRIGHT 1992 ACS

CA101(25):223972y A \*\*\*human\*\*\* \*\*\*parvovirus\*\*\*,  
adeno-associated virus, as a eukaryotic \*\*\*vector\*\*\*: transient  
expression and encapsidation of the prokaryotic gene for  
chloramphenicol acetyltransferase. Tratschin, Jon Duri; West,  
Michael H. P.; Sandbank, Tracey; Carter, Barrie J. (Lab. Cell Biol.  
Genet., Natl. Inst. Arthritis, Genet., Natl. Inst. Arthritis, Diabetes, Dig. Kidney Dis  
., Bethesda,  
MD 20205, USA). Mol. Cell. Biol., 4(10), 2072-81 (Eng) 1984.  
CODEN: MCEBD4. ISSN: 0270-7306.

AB A defective \*\*\*human\*\*\* \*\*\*parvovirus\*\*\*, adeno-assocd.  
virus (AAV), was used as a novel eukaryotic \*\*\*vector\*\*\*  
(parvector) for the expression of a foreign gene in human cells. The  
recombinant, pAV2, contains the AAV genome in a pBR322-derived  
bacterial plasmid. When pAV2 is transfected into human cells  
together with helper adenovirus particles, the AAV genome is rescued  
from the recombinant plasmid and replicated to produce infectious  
AAV particles at high efficiency. To create a \*\*\*vector\*\*\*, a  
prokaryotic sequence coding for chloramphenicol acetyltransferase  
(CAT) [9040-07-7] was inserted into derivs. of pAV2 following  
either of the AAV promoters p40 (pAVHiCAT) and p19 (pAVBcCAT). When  
transfected into human 293 cells or HeLa cells, pAVHiCAT expressed  
CAT activity in the absence of adenovirus. In the presence of  
adenovirus, the \*\*\*vector\*\*\* produced increased amts. of CAT  
activity, and the recombinant AAV-CAT genome was replicated. In 293  
cells, pAVBcCAT expressed a similar amt. of CAT activity in the  
absence or presence of adenovirus, and the recombinant AAV-CAT  
genome was not replicated. In HeLa cells, pAVBcCAT expressed low  
levels of CAT activity, but this level was elevated by coinfection  
with adenovirus particles or by cotransfection with a plasmid which  
expressed the adenovirus early region 1A (E1A) product. The E1A  
product is a transcriptional activator and is expressed in 293  
cells. Thus, expression from 2 AAV promoters is differentially  
regulated; expression from p19 is increased by E1A, whereas p40  
yields high levels of constitutive expression in the absence of E1A.  
Both AAV \*\*\*vectors\*\*\* were packaged into AAV particles by  
complementation with wild-type AAV and yielded CAT activity when  
subsequently infected into cells in the presence of adenovirus.

L19 ANSWER 23 OF 23 COPYRIGHT 1992 ACS

CA101(3):20441b Analysis of proteins, helper dependence, and  
seroepidemiology of a new \*\*\*human\*\*\* \*\*\*parvovirus\*\*\*.  
Georg-Fries, Brigitte; Biederlack, Stefanie; Wolf, Juergen; Zur  
Hausen, Harald (Inst. Virol., Univ. Freiburg, Freiburg D-7800, Fed.  
Rep. Ger.). Virology, 134(1), 64-71 (Eng) 1984. CODEN: VIRLAX.  
ISSN: 0042-6822.

AB A new type of defective parvovirus, tentatively designated as  
adeno-assocd. virus type 5 (AAV-5), is characterized as far as its

proteins, its helper dependence, and its seroepidemiol. are concerned. The protein anal. of AAV-5 in polyacrylamide gels demonstrated the presence of 3 structural polypeptides, corresponding to \*\*\*VP\*\*\*. \*\*\*1\*\*\*, \*\*\*VP\*\*\* \*\*\*2\*\*\*, and VP 3 of other AAV types. The prepn. of monoclonal antibodies against AAV-5 permitted the anal. of viral structural antigen expression by using adenovirus type 12 (Ad 12) or several herpes group viruses as helper viruses, resp. AAV-5-infected cell cultures coinfectd with either Ad 12, herpes simplex virus, cytomegalovirus (CMV), or varicella zoster virus (VZV) efficiently synthesize AAV-5 specific antigens. Epstein-Barr virus and herpes virus saimiri, in contrast, provide only a very weak helper activity for AAV-5 antigen expression. The development of a specific ELISA test permitted screening of human sera for antibodies to AAV-5. Forty-five percent of 926 sera from all age groups and approx. 60% of the adult population reveal antibodies to structural components of this virus. The seroepidemiol. differs from that reported for other AAV serotypes. Highest av. titers against AAV-5 are obsd. in the age group between 15 and 20 yr. Sera from patients with cervical carcinoma revealed av. titers of antibodies well below those of age-matched control groups. Attempts to find higher antibody levels against AAV-5 in specific human diseases failed thus far.

DT J  
CO JGV1AY Best Available Copy  
IS 0022-1317  
PY 1979  
LA Eng  
AB

Poliovirus type 1, vaccine strain (LSc, 2ab), which is a temp.- and actinomycin D-sensitive mutant derived from type 1 Mahoney strain, was grown in HeLa cells with  $^{32}\text{P}$  and a low concn. of actinomycin D. Seven and a half h postinfection (p.i.), genome RNA- $^{32}\text{P}$  was recovered from the purified virion. Anal. of RNase T1 digests of the RNA by 2-dimensional gel electrophoresis revealed that 3 possible point mutation sites exist in the large and unique oligonucleotides in the fingerprint. Neither a capping structure nor a nucleotide such as pppNp, ppNp or pNp, was detected by ion-exchange column chromatog. at pH 5.0 after digestion of virion RNA with RNase T2. Instead, a  $^{32}\text{P}$ -labeled compd. which could be digested with Pronase or proteinase K, was eluted at the void vol. of the column. Proteinase K digests of the  $^{32}\text{P}$ -labeled compd. contained pUp or pU as a single labeled compd. when genome RNA was digested with RNase T2 or nuclease P1, resp, before digestion with the proteinase. The data locate possible point mutation sites on the genome of a mutant strain (LSc, 2ab) of type 1 poliovirus and show that a protein (VPg) is covalently bound to the 5'-terminus of the RNA. The protein (VPg) of LSc, 2ab strain migrates faster than capsid protein VP4 (mol. wt. 7000-8000) in a polyacrylamide gel and is thus similar to the VPg of the wild-type virus.

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(STRINGSEARCH SS 1 :AUTHOR: (AA) )

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# 1 (MEDLINE)

UI - 92393245

AU - Schwarz TF ; Serke S ; Von Brunn A ; Hottentrager B ; Huhn D ;  
Deinhardt F ; Roggendorf M

TI - Heat stability of parvovirus B19: kinetics of inactivation.

AB - Heat inactivation of parvovirus B19 (B19) was studied in a culture of hematopoietic progenitor cells generated in vitro from peripheral human blood. After inoculating cell cultures with identical volumes of plasma (MII) containing B19 (B19-MII) heat-treated (60 degrees C) for various periods of time, a time-dependent inactivation of the input virus was determined by a decrease of viral DNA replication. No B19 DNA was detected after infection with B19-MII heat-treated for 20 min or more by Southern blot. Viral B19 protein production decreased time-dependently and was not detected after infection with samples treated for 12 min at 60 degrees C or more determined by the enzyme immunoassay. This study indicates that infectivity of B19 virus in plasma can be reduced in vitro by heat-treatment (60 degrees C). However, this does not mean that the heat treatment completely inactivated B19 virus.

SO - Int J Med Microbiol Virol Parasitol Infect Dis 1992  
Jul;277(2):219-23

# 2 (MEDLINE)

UI - 92376488

AU - Fridell E ; Bekassy AN ; Larsson B ; Eriksson BM

TI - Polymerase chain reaction with double primer pairs for detection of human parvovirus B19 induced aplastic crises in family outbreaks.

AB - Parvovirus B19 DNA can be detected by polymerase chain reaction with double primer pairs (nested PCR). Recent infection was documented by a retrospective serological study using Parvoscan-B19 enzyme linked immunosorbent assay (EIA) for detection of B19 human parvovirus IgM and IgG antibodies in serum or plasma specimens. In 3 families B19 outbreaks caused aplastic crises necessitating blood transfusion in 5 children and 1 adult with hereditary sphaerocytosis. Four members from 2 of the families had clinically overt haemolytic anaemia prior to the event. Two members in another family presented with an aplastic crisis disclosing the underlying chronic haemolytic disease. All 7 patients were identified as PCR positive in serum samples taken 3-14 days after the onset of symptoms. Comparison with dot blot hybridization revealed detectable DNA in only 2/3 PCR positive patients. Thus, nested PCR is more sensitive than the dot blot hybridization method and is therefore a suitable complement to the antibody assay for identifying recent B19 infection.

SO - Scand J Infect Dis 1992;24(3):275-82

CONTINUE PRINTING? (YES/NO)

USER:

Y

PROG:

# 3 (MEDLINE)

UI - 92368535

AU - Nigro G ; Luzi G ; Fridell E ; Ferrara M ; Pisano P ; Gattinara GC ; Mezzaroma I ; Soderlund M ; Rasnoveanu D ; Aiuti F

TI - Parvovirus infection in children with AIDS: high prevalence of B19-specific immunoglobulin M and G antibodies.

AB - OBJECTIVE: Investigation of the prevalence and pathogenic role of parvovirus B19 infection in Italian and Rumanian children with AIDS, compared with age-matched HIV-negative children (controls) with various recurrent infections of unknown aetiology. DESIGN: Detection of B19-specific immunoglobulin (Ig) M and IgG antibodies as the most indicative markers of past or current B19



infection. METHODS: B19 antibodies were detected by two enzyme immunoassays using synthetic peptide or recombinant protein, which corresponded to different B19 epitopes, as coating antigens. RESULTS: B19 IgM and IgG were seen in 10 out of 20 (50%) Italian and in 20 out of 51 (39.2%) Rumanian children with AIDS, in contrast to none out of 17 Italian and one out of 22 Rumanian controls (P less than 0.001). In addition, two Italian controls (11.8%), two Rumanian children with AIDS (3.9%), and two Rumanian controls (9.1%) had B19 IgM alone. Specific IgG alone was detected in eight (40%) Italian and 14 (27.5%) Rumanian children with AIDS, and in seven (41.2%) Italian and four (10.2%) Rumanian controls. CONCLUSIONS: While it is possible to attribute some B19 infections in Rumanian children to blood transfusion, the source was unknown for Italian children. However, in three of the Italian children who had B19 IgM and IgG persistently for 15-22 months, and in a 2-month-old Italian infant with B19 IgM and IgG, HIV might have activated a congenital or perinatally-acquired B19 infection.

SO - AIDS 1992 Jul;6(7):679-84

CONTINUE PRINTING? (YES/NO)

USER:

y

PROG:

4 (MEDLINE)

UI - 92359182

AU - Kovacs BW ; Carlson DE ; Shahbahrami B ; Platt LD

TI - Prenatal diagnosis of human parvovirus B19 in nonimmune hydrops fetalis by polymerase chain reaction.

AB - OBJECTIVE: Nonimmune hydrops fetalis is a potentially lethal condition reflecting the clinical manifestation of several pathologic processes. Recently maternal infection by human parvovirus B19 has been reported to result in nonimmune fetal hydrops. We sought to develop a rapid and sensitive test to detect the presence of this agent in utero. STUDY DESIGN: Using a cloned isolate of the virus, we developed an assay based on enzymatic amplification of a segment of the human parvovirus B19 genome that allows direct detection of this agent in samples of fetal blood and amniotic fluid. RESULTS: The method detected as few as 100,000 genome equivalences and was specific for the viral genome alone. We used this assay to evaluate nine fetuses initially seen with nonimmune hydrops. Three cases were found to be positive for the human parvovirus B19 genome. CONCLUSION: The method is powerful in that it is rapid, sensitive, and simple. This assay may have general applicability in evaluation of nonimmune hydrops and in documentation of the natural history of fetal human parvovirus infections.

SO - Am J Obstet Gynecol 1992 Aug;167(2):461-6

5 (MEDLINE)

UI - 92359163

AU - Sheikh AU ; Ernest JM ; O'Shea M

TI - Long-term outcome in fetal hydrops from parvovirus B19 infection.

AB - Parvovirus B19 infection in the fetus is associated with anemia and hydrops and can result in fetal death. Fetal transfusion has been used in an attempt to improve outcome; however, it is associated with its own perinatal morbidity. We report two cases of fetal parvovirus B19 infection that were confirmed by polymerase chain reaction for parvovirus B19 deoxyribonucleic acid in umbilical cord blood. Ultrasonographic signs of compromise were observed at 30 and 24 weeks of gestation. Both fetuses were hydropic and one fetus was also anemic. Serial sonograms demonstrated that the hydrops resolved spontaneously over 3 to 5 weeks after diagnosis. One infant was delivered at 32 weeks of gestation as a result of idiopathic preterm labor. The

other infant was delivered at term. Both infants appeared relatively normal at birth and have developed normally in the first year of life. Thus fetal hydrops in association with parvovirus B19 infection does not always lead to poor long-term outcome. A conservative approach without in utero therapy may be appropriate for the management of some of these fetuses.

SO - Am J Obstet Gynecol 1992 Aug;167(2):337-41

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USER:

y

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#### 6 (MEDLINE)

UI - 92356097

AU - Brown KE ; Cohen BJ

TI - Haemagglutination by parvovirus B19.

AB - Human parvovirus B19 is a member of the autonomous parvoviridae but in contrast to other members of the genus has not been shown to agglutinate red blood cells. We now report that the virus agglutinates red cells of primate origin, though with plasma-derived virus this activity is masked by the presence of an IgM-like inhibitor. This observation is consistent with the presence on the erythroid precursor target cell of a specific receptor for parvovirus B19.

SO - J Gen Virol 1992 Aug;73 ( Pt 8):2147-9

#### 7 (MEDLINE)

UI - 92333040

AU - Keeler ML

TI - Human parvovirus B-19: not just a pediatric problem.

AB - Parvoviruses have long been associated with disabling and even fatal illnesses in animals. The discovery of the human parvovirus B-19 in 1975 (1) and subsequent studies of its effects in humans identified this virus as the causative agent of erythema infectiosum ("fifth disease") in children. (2). Erythema infectiosum (EI) is a common, self-limited infectious disorder in children, easily recognized by the classic "slapped cheek: facial erythema and fine reticular rash. Only in the 1980s have further investigations linked HPV B-19 infection with more significant clinical syndromes, among which is an adult polyarthropathy. This presentation in adults is more common than is currently understood and is easily confused with other symmetric polyarthropathies. Recognition and conservative treatment of this disorder are important for the emergency physician, to whom these patients may present.

RF - REVIEW ARTICLE: 17 REFS.

SO - J Emerg Med 1992 Jan-Feb;10(1):39-44

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USER:

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PROG:

#### 8 (MEDLINE)

UI - 92313115

AU - Cope AP ; Jones A ; Brozovic M ; Shafi MS ; Maini RN

TI - Possible induction of systemic lupus erythematosus by human parvovirus.

AB - A 59 year old woman presented with an influenza-like illness preceding signs and symptoms strongly suggestive of systemic lupus erythematosus (SLE), which progressed over several months. Owing to these influenza-like symptoms, a viral cause of her illness was sought. Human parvovirus B19 serology was positive and antibodies to DNA were detected by two different methods. This patient is believed to be the first report of human

parvovirus B19 infection coinciding with the onset of SLE. The evidence for B19 virus and the part it plays in autoimmunity and arthritis is discussed.

SO - Ann Rheum Dis 1992 Jun;51(6):803-4

9 (MEDLINE)

UI - 92300356

AU - Miki NP ; Chantler JK

TI - Non-permissiveness of synovial membrane cells to human parvovirus B19 in vitro.

AB - The ability of cultured human synovial cells derived from synovial membrane and cartilage to support the replication of human parvovirus B19 was assessed. No viral DNA synthesis nor viral antigens were detected suggesting that B19 virus is not capable of replicating in synovial cells. The significance of this finding in relationship to the pathogenesis of parvovirus arthritis is discussed.

SO - J Gen Virol 1992 Jun;73 ( Pt 6):1559-62

CONTINUE PRINTING? (YES/NO)

USER:

y

PROG:

10 (MEDLINE)

UI - 92291324

AU - Rosenfeld SJ ; Yoshimoto K ; Kajigaya S ; Anderson S ; Young NS ; Field A ; Warren P ; Bansal G ; Collett MS

TI - Unique region of the minor capsid protein of human parvovirus B19 is exposed on the virion surface.

AB - Capsids of the B19 parvovirus are composed of major (VP2; 58 kD) and minor (VP1; 83 kD) structural proteins. These proteins are identical except for a unique 226 amino acid region at the amino terminus of VP1. Previous immunization studies with recombinant empty capsids have demonstrated that the presence of VP1 was required to elicit virus-neutralizing antibody activity. However, to date, neutralizing epitopes have been identified only on VP2. Crystallographic studies of a related parvovirus (canine parvovirus) suggested the unique amino-terminal portion of VP1 assumed an internal position within the viral capsid. To determine the position of VP1 in both empty capsids and virions, we expressed a fusion protein containing the unique region of VP1. Antisera raised to this protein recognized recombinant empty capsids containing VP1 and VP2, but not those containing VP2 alone, in an enzyme-linked immunosorbent assay. The antisera immunoprecipitated both recombinant empty capsids and human plasma-derived virions, and agglutinated the latter as shown by immune electron microscopy. The sera contained potent neutralizing activity for virus infectivity in vitro. These data indicate that a portion of the amino terminus of VP1 is located on the virion surface, and that this region contains intrinsic neutralizing determinants. The external location of the VP1-specific tail may provide a site for engineered heterologous epitope presentation in novel recombinant vaccines.

SO - J Clin Invest 1992 Jun;89(6):2023-9

CONTINUE PRINTING? (YES/NO)

USER:

y

PROG:

11 (MEDLINE)

UI - 92271081

AU - Rollag H ; Patou G ; Pattison JR ; Degre M ; Evensen SA ; Frøland SS ; Glomstein A

TI - Prevalence of antibodies against parvovirus B19 in Norwegians

- with congenital coagulation factor defects treated with plasma products from small donor pools.
- AB - The seroprevalence of antibodies against parvovirus B19 in 308 Norwegians with coagulation factor defects of different types and severities was assessed by an IgG antibody capture radioimmunoassay (GACRIA). The overall seroprevalence was 62%. The seroprevalence among subjects with different types of coagulation factor defects was related to the type and severity of the coagulation factor defect: severe hemophilia A 64%, moderate and mild hemophilia A 58%, severe hemophilia B 88%, moderate and mild hemophilia B 73%, and von Willebrand's disease 52%. The prevalence of parvovirus B19 antibodies among household contacts and blood donors was 49% and 42% respectively. This study confirms that replacement therapy with coagulation factors is accompanied by an increased risk for acquiring parvovirus B19 infection. However, the prevalence of parvovirus B19 antibodies among Norwegian hemophiliacs is well below the prevalence reported from other countries and probably reflects the small numbers of donors in plasma pools used for the preparation of coagulation factor concentrates.
- SO - Scand J Infect Dis 1991;23(6):675-9

12 (MEDLINE)

- UI - 92260184
- AU - Sosa CE ; Mahony JB ; Luinstra KE ; Sternbach M ; Chernesky MA
- TI - Replication and cytopathology of human parvovirus B19 in human umbilical cord blood erythroid progenitor cells.
- AB - Human parvovirus B19 productively infected erythroid progenitor (EP) cells from umbilical cord blood, in vitro as shown by an increase of viral DNA in supernatant fluid assayed by dot blot hybridization and liquid scintillation counting. Progeny virus was released into the supernatant fluid of CD34+ EP cells which had been purified by immunomagnetic separation. This supernatant fluid was infectious for bone marrow cells. Erythroid bursts infected with virus showed characteristic cytopathic effect by electron microscopy consisting of cytoplasmic vacuolization, marginated chromatin, and nuclear inclusions of lattice or crystalline arrays. Cultures of umbilical cord blood EP cells may be useful for the propagation of parvovirus B19 serological testing reagents and the study of virus-host cell interactions.
- SO - J Med Virol 1992 Feb;36(2):125-30
- CONTINUE PRINTING? (YES/NO)

USER:

Y

PROG:

13 (MEDLINE)

- UI - 92248254
- AU - Schwarz TF ; Hottentrager B ; Roggendorf M
- TI - Prevalence of antibodies to parvovirus B19 in selected groups of patients and healthy individuals.
- AB - The prevalence of antibodies to parvovirus B19 in sera (n = 745) of various groups of patients and healthy individuals was determined by the enzyme immunoassay, using viral particles as antigen. Among healthy individuals, anti-B19 IgG prevalence was highest in nurses (65.4% (17/26)); in medical students it was 34.1% (47/138) and in pregnant females, 24.4% (48/197). 37.0% (44/119) of HIV-negative haemophilic patients and 91.7% (33/36) of haemophilic patients with HIV infection were anti-B19 IgG-positive. 45.8% (55/120) of dialysis patients and 27.5% (30/109) of patients with asymptomatic HIV infection were positive for anti-B19 IgG. With the exception of HIV-infected haemophilic patients, no specific "risk group" for B19 infection could be identified.
- SO - Int J Med Microbiol Virol Parasitol Infect Dis 1992

## 14 (MEDLINE)

UI - 92239559

AU - Torok TJ ; Wang QY ; Gary GW Jr ; Yang CF ; Finch TM ; Anderson LJ

TI - Prenatal diagnosis of intrauterine infection with parvovirus B19 by the polymerase chain reaction technique.

AB - Human parvovirus B19 is a recently recognized cause of fetal hydrops and death. Efforts to characterize the natural history of fetal infection with this virus have been hampered by the lack of sensitive and specific tests for diagnosis in utero. Using the highly sensitive polymerase chain reaction (PCR) assay, we determined the fetal infection status in 56 pregnancies by testing amniotic fluid, fetal serum, and maternal serum for B19 DNA and antibodies. Factors associated with a high risk of B19 infection were fetal disease, exposure to persons with erythema infectiosum, or signs or symptoms of acute B19 infection. Fifteen women (27%) were B19 IgM-positive, a status suggesting recent infection; the positivity of all of the corresponding fetal specimens for B19 DNA in the PCR was indicative of fetal infection. In four of these cases, serial ultrasonographic examinations documented spontaneous resolution of fetal hydrops. Twenty-four women (43%) were IgG-positive and IgM-negative; this pattern suggested prior infection. The PCR gave positive results, consistent with recent maternal infection, in four of these cases. Seventeen women (30%) were IgG-negative and IgM-negative, a pattern suggesting no prior infection; the PCR results in four cases were indicative of a possible early maternal infection or a possible atypical immune response. The PCR is a sensitive and rapid method for the diagnosis of intrauterine infection with human parvovirus B19 and promises to facilitate studies of the natural history and treatment of this infection.

SO - Clin Infect Dis 1992 Jan;14(1):149-55

CONTINUE PRINTING? (YES/NO)

USER:

Y

PROG:

## 15 (MEDLINE)

UI - 92228402

AU - Pryde PG ; Nugent CE ; Pridjian G ; Barr M Jr ; Faix RG

TI - Spontaneous resolution of nonimmune hydrops fetalis secondary to human parvovirus B19 infection.

AB - Many instances of nonimmune hydrops fetalis ascribed to human parvovirus B19 have been reported. The leading proposed pathophysiologic mechanism of hydrops in affected fetuses is viral invasion of red blood cell progenitors, causing a profound reticulocytopenic fetal anemia. Although the natural history of fetal parvovirus infection remains to be elucidated fully, there have been recent reports of funipuncture and intrauterine blood transfusions to diagnose and manage this problem. We report two pregnancies in which parvovirus-related hydrops fetalis was observed to resolve without intervention, followed by uncomplicated vaginal deliveries of healthy infants. These observations emphasize the need for further investigation before recommending routine fetal blood transfusion in affected cases.

SO - Obstet Gynecol 1992 May;79(5 ( Pt 2)):859-61

## 16 (MEDLINE)

UI - 92219044

AU - Morey AL ; O'Neill HJ ; Coyle PV ; Fleming KA

TI - Immunohistological detection of human parvovirus B19 in formalin-fixed, paraffin-embedded tissues.

AB - Human parvovirus B19 is a cause of aplastic crises in patients

with haemolytic anaemias, prolonged bone marrow failure in the immunosuppressed, and fetal death secondary to non-immune hydrops. The immunohistological detection of parvovirus B19 in formalin-fixed, paraffin-embedded tissues has not previously been reported, and definitive diagnosis of infection in such specimens has relied on the use of specialized DNA hybridization and amplification techniques. A new monoclonal antibody to B19 capsid proteins, R92F6, was found to be capable of labelling infected cells in paraffin-embedded tissues from all 19 cases of parvovirus-related fetal hydrops tested, and in bone marrow from a child with congenital immunodeficiency and chronic parvovirus infection. Viral antigen was detected both in cytoplasmic and in nuclear distributions using the alkaline phosphatase anti-alkaline phosphatase (APAAP) technique without preceding proteolytic digestion. The viral epitope recognized appears to be highly conserved, as specimens were obtained over a 13-year period from widely spaced locations in the U.K. Antibody R92F6 should facilitate rapid diagnosis of parvovirus B19 infection in routinely processed and archival specimens.

SO - J Pathol 1992 Feb;166(2):105-8

CONTINUE PRINTING? (YES/NO)

USER:

y

PROG:

17 (MEDLINE)

UI - 92198218

AU - O'Neill HJ ; Coyle PV

TI - Two anti-parvovirus B 19 IgM capture assays incorporating a mouse monoclonal antibody specific for B 19 viral capsid proteins VP 1 and VP 2.

AB - During an outbreak of parvovirus B 19 in 1989 in Northern Ireland, 7580 blood donors were screened for B 19 antigen. Two units screened positive, one of which was obtained for use as viral antigen. A monoclonal antibody (R92F6) made against this antigen was specific for B 19 capsid proteins VP 1 and VP 2. The monoclonal antibody was used in the development of 2 anti-B 19 IgM capture enzyme assays. These used a conventional substrate (O-phenylene diamine) and a chemiluminescent signal reagent. There was excellent concordance between the 2 assays. A total of 403 patients sera were tested and 65 sera were positive in each assay.

SO - Arch Virol 1992;123(1-2):125-34

18 (MEDLINE)

UI - 92179524

AU - Yun ZB ; Hornsleth A

TI - Production of digoxigenin-labelled parvovirus DNA probe by PCR.

AB - A 560-bp digoxigenin(Dig)-labelled DNA-probe was produced by PCR using a 699-bp parvovirus DNA fragment as template with introduction of Dig-dTUP into the PCR reaction mixture. It was found to be very important to pay close attention to the amount of template employed, the number of cycles used, predenaturation of target DNA and optimization of the percentage of dTTP substituted by Dig-DUTP in the reaction mixture. The same 560-bp DNA fragment produced by PCR without the incorporation of Dig-DUTP in the reaction mixture, was subsequently labelled with Dig-dTUP by the random primed labelling method. Both of the Dig-labelled parvovirus DNA probes described above showed the same DNA detection level (about 1 pg), but production of the probe with Dig-DUTP incorporated in the PCR reaction mixture was much simpler.

SO - Res Virol 1991 Jul-Aug;142(4):277-81

CONTINUE PRINTING? (YES/NO)

USER:  
Y  
PROG:

19 (MEDLINE)

UI - 92165938  
AU - Söderlund M ; Brown KE ; Meurman O ; Hedman K  
TI - Prokaryotic expression of a VP1 polypeptide antigen for diagnosis by a human parvovirus B19 antibody enzyme immunoassay.  
AB - To produce parvovirus B19 antigen for diagnostic purposes, partially overlapping segments covering the genes encoding the viral structural proteins VP1 and VP2 were cloned into expression vectors. The constructs were induced in Escherichia coli, resulting in the expression of beta-galactosidase fusion proteins. In immunoblotting experiments with sera from patients with erythema infectiosum, immunoglobulin G (IgG) and IgM antibodies bound to a single polypeptide of 235 amino acids at the N terminus of VP1. The DNA fragment encoding this polypeptide was amplified by the polymerase chain reaction and cloned into an expression vector. The viral capsid antigen expressed in E. coli was purified by preparative agarose gel electrophoresis and used in IgG and IgM solid-phase enzyme immunoassays. Comparison with reference gamma- and mu-capture radioimmunoassays using whole virus antigen showed that these antibody tests are suitable for the serodiagnosis of human infections caused by parvovirus B19.  
S0 - J Clin Microbiol 1992 Feb;30(2):305-11

20 (MEDLINE)

UI - 92129620  
AU - Musiani M ; Zerbini M ; Gibellini D ; Gentilomi G ; Venturoli S ; Gallinella G ; Ferri E ; Girotti S  
TI - Chemiluminescence dot blot hybridization assay for detection of B19 parvovirus DNA in human sera.  
AB - A chemiluminescence dot blot hybridization assay was used for the detection of B19 parvovirus DNA in human sera by using digoxigenin-labeled probes. The probes were revealed immunoenzymatically by use of anti-digoxigenin Fab fragments conjugated with alkaline phosphatase. The chemiluminescence signal was obtained by reacting the labeled probe-target complex with an enzyme-triggerable dioxetane substrate. The emitted photons were detected with instant photographic films. In the search for B19 parvovirus DNA, 2,808 serum samples were analyzed.  
S0 - J Clin Microbiol 1991 Sep;29(9):2047-50  
CONTINUE PRINTING? (YES/NO)

USER:  
Y  
PROG:

21 (MEDLINE)

UI - 92114159  
AU - Schwarz TF ; Serke S ; Hottenträger B ; von Brunn A ; Baurmann H ; Kirsch A ; Stolz W ; Huhn D ; Deinhardt F ; Roggendorf M  
TI - Replication of parvovirus B19 in hematopoietic progenitor cells generated in vitro from normal human peripheral blood.  
AB - Erythroid progenitor cells generated in vitro from peripheral human blood in the presence of interleukin-3 and erythropoietin were infected with human parvovirus B19. B19 virus DNA replication was highest 48 to 72 h after infection, and maximum levels of B19 virus proteins were detected in culture supernatants at 72 to 96 h after infection. B19 virus propagated in vitro was infectious. This cell culture system with peripheral blood cells facilitates studies in vitro of B19 virus replication.  
S0 - J Virol 1992 Feb;66(2):1273-6

22 (MEDLINE)

UI - 92113594

AU - Field AM ; Cohen BJ ; Brown KE ; Mori J ; Clewley JP ; Nascimento JP ; Hallam NF

TI - Detection of B19 parvovirus in human fetal tissues by electron microscopy.

AB - We present the electron microscopy observations on samples from 38 pregnancies that were investigated for B19 parvovirus infection. Thirty-four had resulted in fetal loss thought to be due to a virus infection and 22 of the 38 were positive for B19 parvovirus in one or more of the tissues. Twenty-one placentas and 75 fetal tissue samples were examined. Fresh samples were investigated by immune electron microscopy while formalin-fixed tissues were examined as thin sections and by negative staining of tissue extracts with direct electron microscopy. Electron microscopy was more sensitive on fresh than on fixed samples. The ultrastructural observations on thin sections of fixed tissues yielded new information locating B19 parvovirus particles in both nucleus and cytoplasm of infected fetal cells. The diagnostic results of the range of electron microscopy assays were compared with those of two hybridization methods. The fresh samples yielded comparable results from electron microscopy and hybridisation assays but on formalin-fixed materials hybridisation was more sensitive.

S0 - J Med Virol 1991 Oct;35(2):85-95

CONTINUE PRINTING? (YES/NO)

USER:

y

PROG:

23 (MEDLINE)

UI - 92113585

AU - Erdman DD ; Usher MJ ; Tsou C ; Caul EO ; Gary GW ; Kajigaya S ; Young NS ; Anderson LJ

TI - Human parvovirus B19 specific IgG, IgA, and IgM antibodies and DNA in serum specimens from persons with erythema infectiosum.

AB - To determine the diagnostic use of different markers of acute parvovirus B19 infection, serum specimens obtained from 128 persons with erythema infectiosum were tested for specific immunoglobulin G (IgG), IgA, and IgM antibodies by capture enzyme immunoassay (EIA) using Chinese hamster ovary (CHO) cell-expressed B19 antigen, and tested for circulating B19 DNA by polymerase chain reaction (PCR). A significant rise in specific IgG and IgA antibodies was detected in 87% and 77%, respectively, of persons from whom acute- and convalescent-phase serum specimens were available. Specific IgA antibodies were detected in single serum specimens from 90% of cases and were present in 22 (18%) of 120 persons from a control group without a history of recent exposure to B19. Specific IgM antibodies were detected in 97% of cases and one person (1%) from the control group. B19 DNA was detected in 94% of cases and was absent in 20 persons from the control group positive for both IgG and IgA antibodies. Serum specimens obtained between 4 and 6 months after onset of illness from six additional persons were also tested. All had specific IgG antibodies, four (67%) had IgA, five (83%) had IgM, and none had detectable B19 DNA. Our data indicate that 1) specific IgA antibodies are too persistent to be a useful indicator of recent B19 infection; 2) specific IgM antibodies are the most sensitive indicator of acute B19 infection in immunologically normal persons but can persist up to 6 months; and 3) B19 DNA can often be detected up to 2 months after onset of illness even in immunologically normal hosts and might be a useful adjunct test for diagnosis of acute B19 infection.

S0 - J Med Virol 1991 Oct;35(2):110-5

CONTINUE PRINTING? (YES/NO)



USER:  
Y  
PROG:

24 (MEDLINE)

UI - 92096603  
AU - Shimomura S ; Komatsu N ; Frickhofen N ; Anderson S ; Kajigaya S ; Young NS  
TI - First continuous propagation of B19 parvovirus in a cell line.  
AB - The pathogenic human parvovirus B19 has extreme tropism for human erythroid progenitor cells and has resisted cultivation in conventional cell lines. We report first propagation of this virus in an erythropoietin-dependent strain of a megakaryoblastic leukemia cell line called UT-7. Virus protein was present in about 5% of cells after 1 week of culture. Appropriate ratios of major and minor capsid proteins were determined by immunoblot, and newly synthesized capsid protein was detected by immunoprecipitation of radioactively labeled cell lysates. High molecular weight monomer and dimer intermediates were detected by Southern analysis, indicating active viral replication. Approximately 1,000 genome copies were present per infected cell, and at the optimal multiplicity of infection 20- to 50-fold more virus was produced than inoculated. Virus propagation only occurred in UT-7 cells that were adapted to growth in erythropoietin; virus signal was not detected in UT-7 cells adapted for growth in granulocyte-macrophage colony-stimulating factor or interleukin-3, even with exposure to erythropoietin for several days. Infectious virus was detected in cultures as long as 3 months after inoculation. Despite persistence, there was no evidence of viral integration on Southern analysis. This cell line may prove useful for the production of infectious virus and in the analysis of B19 parvovirus persistence, cytotoxicity, and permissivity.  
SO - Blood 1992 Jan 1;79(1):18-24  
CONTINUE PRINTING? (YES/NO)

USER:  
Y  
PROG:

25 (MEDLINE)

UI - 92087275  
AU - Teuscher T ; Baillod B ; Holzer BR  
TI - Prevalence of human parvovirus B19 in sickle cell disease and healthy controls.  
AB - The serological HPV status of 35 patients with SCA (Hb SS), randomly chosen from a sickle cell clinic in rural south-west Togo and of 13 household members with normal haemoglobin type (Hb AA) was assessed. No difference in HPV-IgG seropositivity rate was found. In 30 urban hospital patients from Abidjan, Ivory Coast, who were in acute painful sickle cell crisis HPV-IgG seropositivity rate increased with age. In only one (HIV positive) patient HPV-IgM antibodies were detected. It is concluded that HPV-infection exists in West Africa (1) and that there is no evidence for increased seroprevalence in SCA (2). HPV does not seem to trigger acute painful crises in SCA (3). The age-specific HPV seropositivity increase in urban patients may be due to differing transmission rates in urban and rural areas.  
SO - Trop Geogr Med 1991 Jan-Apr;43(1-2):108-10

26 (MEDLINE)

UI - 92078381  
AU - Prato C ; Paper T ; Morinet F  
TI - Use of M13 single-stranded DNA digoxigenin labelled probe for detection of human parvovirus B19 viraemia.

AB - A dot-blot hybridization assay for serum B19 DNA is described using a non-radioactive (digoxigenin) M13 single-stranded DNA probe. The assay is sensitive (0.3 pg of B19 DNA) and has several advantages over similar assays which use radioactive or non-radioactive labelled plasmid probe for the routine detection of B19 DNA in sera.

S0 - J Virol Methods 1991 Oct;34(3):227-31

CONTINUE PRINTING? (YES/NO)

USER:

y

PROG:

27 (MEDLINE)

UI - 92044483

AU - Schwarz TF ; Roggendorf M ; Hottentrager B ; Stolz W ; Schwinn H

TI - Removal of parvovirus B19 from contaminated factor VIII during fractionation.

AB - A solution of pooled cryo-precipitate for preparing factor VIII (F VIII) by the solvent/detergent method was contaminated experimentally with parvovirus B19-positive plasma to evaluate virus reduction achieved by the final steps of the F VIII production process. Virus reduction was at least 2 logs of the total amount of B19 virus added to the pooled cryo-precipitate. The major amount of B19 virus was detected in the solution used to regenerate the F VIII-selective anion exchange chromatography column. A few viral particles were detected in the final F VIII concentrate before filtration but these were aggregates and were removed by filtration, and in the solution used to regenerate the anion exchange resin. It is not known whether the residual viral DNA present in the final product represents infectious or inactivated particles.

S0 - J Med Virol 1991 Sep;35(1):28-31

28 (MEDLINE)

UI - 92008070

AU - Gahr M ; Pekrun A ; Eiffert H

TI - Persistence of parvovirus B19-DNA in blood of a child with severe combined immunodeficiency associated with chronic pure red cell aplasia.

AB - In a female child with severe combined immunodeficiency, pure red cell aplasia was observed which required regular transfusions of erythrocytes. Parvovirus B 19 DNA (but no antibodies) was detected in stored serum samples after the death of the patient. We suggest that the anaemia was a consequence of parvovirus infection which persisted for at least 2 years due to the immunodeficiency.

S0 - Eur J Pediatr 1991 May;150(7):470-2

SS 2 /C?

USER:

prt ar compressed

PROG:

1 (BIOTECHSEEK)

UI - 90329218

AU - Dixit M ; Tillery MK ; Plonk SG ; Ohi S

TI - The recombinant human parvoviruses for gene therapy of hemoglobinopathies.

AB - Towards a goal of using adeno-associated viruses (AAV), the human parvovirus, as the gene transfer vector for gene therapy of hemoglobinopathies, the human beta-globin (h beta G) cDNA was ligated downstream of the P40 promoter of AAV type 2 (AAV2) genome. Transfection via electroporation of the construct into human 293 cells (embryonal kidney cell line) resulted in expression of the cloned h beta G cDNA, as evidenced by the

synthesis of transcripts hybridizable to h beta G probe. The transfection led to the recombinant genome to be excised out of the plasmid and replicate in the cell, followed by production of the recombinant AAV that harbors h beta G cDNA.

S0 - SAAS Bull Biochem Biotechnol 1990 Jan;3:63-8

SS 3 /C?

USER:

display &-mfs-&

PROG:

SEARCH FORMULATION BEGINNING AT SS 1 :

(PARVOVIRUS B19, HUMAN )

SEARCH FORMULATION BEGINNING AT SS 2 :

(EXPLODE VACCINES.: (MN) )

SEARCH FORMULATION BEGINNING AT SS 3 :

(SS 1 AND SS 2 )

NO SUBHEADINGS APPLIED TO ANY SEARCH STATEMENT.

SS 2 /C?

USER:

display

PROG:

SEARCH FORMULATION BEGINNING AT SS 1 :

(SS 1(RESTACKED) AND SS 2(RESTACKED) ) -- 2 ITEMS FOUND IN MEDLINE

NO SUBHEADINGS APPLIED TO ANY SEARCH STATEMENT.

SS 2 /C?

USER:

prt ar compressed

PROG:

1 (MEDLINE)

UI - 92251115

AU - Reves RR ; Pickering LK

TI - Impact of child day care on infectious diseases in adults.

AB - The authors review diseases that occur in day care centers and their impact on day care providers and parents. Acute infections of the gastrointestinal and respiratory tracts are the most commonly transmitted illnesses from children in day care centers to adults. The most important infections acquired by adults are those with the potential for significant clinical morbidity, such as hepatitis A, or those that generate concern, such as cytomegalovirus and parvovirus B19, because of their potential to produce congenital infections in pregnant women.

RF - REVIEW ARTICLE: 60 REFS.

S0 - Infect Dis Clin North Am 1992 Mar;6(1):239-50

2 (MEDLINE)

UI - 92137806

AU - Wiersbitzky S ; Bruns R

TI - [Human Parvovirus B19--really only fifth disease? Unusual disease course in children and adolescents]

AB - The human parvovirus B19 agent causes infectious erythema (fifth disease). However, a wide range of other pathological

manifestations may also be seen: atypical exanthema, ARD (also obstructive forms, e.g. bronchiolitis), acute gastroenteritis, chronic anemia or aplastic crises (in constitutional or malignant hematological diseases or immunological deficiency), arthralgia/arthritis (e.g. rheumatoid arthritis, jcA), diseases of the central nervous systems (e.g. febrile convulsions in young children), lymphadenopathies (e.g. lymphadenitis mesenterialis or pseudoappendicitis); prenatal infection can lead to fetal death (not malformations!). Infection occurring concomitantly with vaccination may suggest complications of the latter. To clarify the true etiological situation, modern laboratory investigations are then required. Vaccination against parvovirus B19 (initially indicated in the case of non-immune girls and women wanting children) is a desirable future development.

RF - REVIEW ARTICLE: 20 REFS.

S0 - Fortschr Med 1991 Dec 20;109(36):729-32

SS 2 /C?

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(FILE 'USPAT' ENTERED AT 14:39:06 ON 27 NOV 92)

L1 97 S PARVOVIRUS? OR PARVOVIRIDAE OR PARVOVIRAL  
L2 96252 S HUMAN OR B19  
L3 66 S L1(L)L2  
L4 2 S L1(1A)L2  
L5 49 S L3 AND (VACCIN? OR IMMUNIZ? OR IMMUNIS?)

L6 12912 S SPODPTER? OR FRUGIPERD? OR LEPIDOPTER? OR BACULOVIR? OR  
ES  
L7 40 S L1 AND L6  
L8 0 S L7 AND B19  
L9 0 S L1 AND B19  
L10 3 S L1 AND (VP1 OR VP2)  
L11 5 S L4 OR L10

=> d l11 1-5 leg,kwic

US PAT NO: 5,139,941 [IMAGE AVAILABLE] L11: 1 of 5  
DATE ISSUED: Aug. 18, 1992  
TITLE: AAV transduction vectors  
INVENTOR: Nicholas Muzyczka, Stony Brook, NY  
Paul L. Hermonat, Bethesda, MD  
Kenneth I. Berns, Mamaroneck, NY  
Richard J. Samulski, Princeton, NJ  
ASSIGNEE: University of Florida Research Foundation, Inc., Alachua,  
FL (U.S. corp.)  
APPL-NO: 07/785,224  
DATE FILED: Oct. 25, 1991  
ART-UNIT: 185  
PRIM-EXMR: James Martinell  
LEGAL-REP: Kerkam, Stowell, Kondracki & Clarke

US PAT NO: 5,139,941 [IMAGE AVAILABLE] L11: 1 of 5

SUMMARY:

BSUM(4)

Adeno-associated virus-2 (AAV) is a human parvovirus which can  
be propagated both as a lytic virus and as a provirus [Cukor et al, In:  
The Paroviruses, ed.. . .

US PAT NO: 5,080,896 [IMAGE AVAILABLE] L11: 2 of 5  
DATE ISSUED: Jan. 14, 1992  
TITLE: Synthetic immunogen  
INVENTOR: Nicolaas Visser, Boxmeer, Netherlands  
Petrus J. Boon, Oss, Netherlands  
ASSIGNEE: Akzo N. V., Arnhem, Netherlands (foreign corp.)  
APPL-NO: 07/191,801  
DATE FILED: May 6, 1988  
ART-UNIT: 181  
PRIM-EXMR: Jefrey E. Russel  
ASST-EXMR: Kay Kim  
LEGAL-REP: William M. Blackstone

US PAT NO: 5,080,896 [IMAGE AVAILABLE] L11: 2 of 5

DETDESC:

DETD(26)

Parvovirus Immunogen

DETDESC:

DETD(27)

A. Preparation of Porcine Parvovirus Antigen

DETDESC:

DETD(28)

A 65 kD coat protein of porcine parvovirus (PPV) is isolated in accordance with the procedure described by Molitor, T. W., Joo, H. S. and Collet, M. S.:

DETD(29)

DETD(34)

#### B. Derivatisation of Porcine Parvovirus Antigen

DETD(35)

DETD(42)

#### Parvovirus Peptide Immunogen

DETD(43)

DETD(50)

#### Parvovirus Immunogen

DETD(44)

DETD(53)

#### B. Preparation of Derivatized Porcine- Parvovirus antigen

DETD(45)

DETD(54)

A solution of the parvovirus protein (2 mg), isolated as described under Example 4A, in 0.1 mol/l sodiumphosphate, pH 7.6, is treated with N-succinimidyl 3-(2-pyridyldithio)-propionate.

DETD(46)

DETD(56)

A . . . (containing 0.6 .mu.mol of free thiol groups), obtained as described under A, is added to a solution of 2-pyridyldisulfide-substituted porcine parvovirus protein (containing 0.45 .mu.moles at 2-pyridyldisulfide groups), obtained as described under B.

DETD(47)

DETD(105)

#### A. Preparation Of A Porcine Parvovirus Peptide

DETD(48)

DETD(106)

A porcine parvovirus (ppv) 15-peptide derivative-- ##STR4## the sequence of which corresponds with a very hydrophilic region on a ppv coat protein VP1 , is prepared by solid phase peptide synthesis on a VEGA Coupler 250 C automated synthesizer. The synthesis is started with.

TITLE: Adeno-associated virus as eukaryotic expression vector  
INVENTOR: Barrie J. Carter, Kensington, MD  
Jon D. Tratschin, Berne, Switzerland  
ASSIGNEE: The United States of America as represented by the  
Department of Health and Human Services, Washington, DC  
(U.S. govt.)  
APPL-NO: 06/712,236  
DATE FILED: Mar. 15, 1985  
ART-UNIT: 105  
PRIM-EXMR: Thomas G. Wiseman  
ASST-EXMR: Stephanie Seidman  
LEGAL-REP: Holman & Stern

US PAT NO: 4,797,368 L11: 3 of 5

DETD(3)

Vectors . . . viruses. Examples of such DNA viruses include papovavirus, adenovirus, herpesvirus, poxvirus and the like. Among the DNA viruses the defective, human parvovirus designated adeno-associated virus (AAV) is a novel eukaryotic vector (parvector) for the expression of foreign genes in human, mammalian and . . .

DETD(4)

As noted above, AAV is a defective human parvovirus and grows only in cells which are also infected with a helper virus (adenovirus or herpesvirus). Replication of AAV is. . .

US PAT NO: 4,563,419 L11: 4 of 5  
DATE ISSUED: Jan. 7, 1986  
TITLE: Detection of microbial nucleic acids by a one-step sandwich hybridization test  
INVENTOR: Tuula M. Ranki, Espoo, Finland  
Hans E. Soderlund, Espoo, Finland  
ASSIGNEE: Orion Corporation Ltd., Espo, Finland (foreign corp.)  
APPL-NO: 06/566,532  
DATE FILED: Dec. 29, 1983  
ART-UNIT: 127  
PRIM-EXMR: Thomas G. Wiseman  
ASST-EXMR: M. Moskowitz  
LEGAL-REP: Brumbaugh, Graves, Donohue & Raymond

US PAT NO: 4,563,419 L11: 4 of 5

SUMMARY:

BSUM(22)

(b) Viruses: rotaviruses, parvoviruses, adenoviruses, enteroviruses

DETD(16)

The . . . areas coding for both early and late messengers. Thus fragment B contained about 700 bases from the structural protein gene VP1 and over 600 bases from the gene for early messengers. Because the DNA of SV40 virus is in itself a. . .

US PAT NO: 4,486,539 L11: 5 of 5



DATE ISSUED: Dec. 4, 1984  
TITLE: Detection of microbial nucleic acids by a one-step  
sandwich hybridization test  
INVENTOR: Tuula M. Ranki, Espoo, Finland  
Soderlund Hans E., Espoo, Finland  
ASSIGNEE: Orioon Corporation Ltd., Finland (foreign corp.)  
APPL-NO: 06/434,182  
DATE FILED: Oct. 14, 1982  
ART-UNIT: 223  
PRIM-EXMR: Christine M. Nucker  
ASST-EXMR: M. Moskowitz  
LEGAL-REP: Brumbaugh, Graves, Donohue & Raymond

US PAT NO: 4,486,539

L11: 5 of 5

SUMMARY:

BSUM(19)

(b) Viruses: rotaviruses, parvoviruses, adenoviruses, enteroviruses

DEDESC:

DETD(28)

The . . . areas coding for both early and late messengers. Thus  
fragment B contained about 700 bases from the structural protein gene  
VP1 and over 600 bases from the gene for early messengers. Because  
the DNA of SV40 virus is in itself a. . .

=>

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=> e kajigaya/au
E1      2      KAJIGAWA, AKIRA/AU
E2      1      KAJIGAWA, SATOSHI/AU
E3      0 --> KAJIGAYA/AU
E4      3      KAJIGAYA, HIROMI/AU
E5      1      KAJIGAYA, HIROSHI/AU
E6      4      KAJIGAYA, ICHIRO/AU
E7     19      KAJIGAYA, SACHIKO/AU
E8      2      KAJIGAYA, TOMIO/AU
E9      1      KAJIGAYA, YASUHIKO/AU
E10     2      KAJIGAYA, YOSHIHIRO/AU
E11     1      KAJIGUCHI, OSAMU/AU
E12     1      KAJIHARA, A/AU
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=> s e7
L1      19 "KAJIGAYA, SACHIKO"/AU
```

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=> display
ENTER (L1), L# OR ?:11
ENTER ANSWER NUMBER OR RANGE (1):1-19
ENTER DISPLAY FORMAT (BIB):bib,ab
```

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L1      ANSWER 1 OF 19  COPYRIGHT 1992 ACS
AN      CA117(9):83068m
TI      Herbimycin A, an inhibitor of tyrosine kinase, prolongs survival of
        mice inoculated with myeloid leukemia C1 cells with high expression
        of v-abl tyrosine kinase
AU      Homma, Yoshio; Okabe-Kado, Junko; Kasukabe, Takashi; Hozumi, Motoo;
        Kodama, Hiroaki; Kajigaya, Sachiko; Suda, Toshio; Miura, Yoshisada
CS      Dep. Chemother., Saitama Cancer Cent. Res. Inst.
LO      Saitama 362, Japan
SO      Cancer Res., 52(14), 4017-20
SC      1-6 (Pharmacology)
DT      J
CO      CNREA8
IS      0008-5472
PY      1992
LA      Eng
AB      Herbimycin A, a benzoquinonoid ansamycin antibiotic, reduces
        intracellular phosphorylation by some tyrosine kinases, including
        v-abl. The mouse megakaryoblastic cell line C1 expresses v-abl
        protein at high levels. Herbimycin A at about 20 ng/mL caused 50%
        inhibition of growth of C1 cells but at 100 ng/mL scarcely affected
        the growth of another mouse leukemia cell line, M1 cells, or of
        normal bone marrow cells. Injection of 106 C1 cells into nude mice
        resulted in death of all the mice within 30 days. Administration of
        herbimycin A significantly enhanced the survival of mice inoculated
        with C1 cells but scarcely affected the survival of mice inoculated
        with M1 cells. These results suggest that herbimycin A and/or
        related compds. may be useful for treatment of some types of
        leukemia in which tyrosine kinase activity is implicated as a
        determinant of the oncogenic state.
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L1      ANSWER 2 OF 19  COPYRIGHT 1992 ACS
AN      CA117(7):65078k
TI      Unique region of the minor capsid protein of human parvovirus B19 is
        exposed on the virion surface
AU      Rosenfeld, Stephen J.; Yoshimoto, Kohji; Kajigaya, Sachiko;
        Anderson, Stacie; Young, Neal S.; Field, Anne; Warrenner, Paul;
        Bansal, Geetha; Collett, Marc S.
CS      Cell Biol. Sect., Natl. Heart, Lung and Blood Inst.
LO      Bethesda, MD 20817, USA
SO      J. Clin. Invest., 89(6), 2023-9
```

SX 10  
DT J Best Available Copy

CO JCINAO  
IS 0021-9738  
PY 1992  
LA Eng

AB Capsids of the B19 parvovirus are composed of major (VP2; 58 kD) and minor (VP1; 83 kD) structural proteins. These proteins are identical except for a unique 226 amino acid region at the amino terminus of VP1. Previous immunization studies with recombinant empty capsids have demonstrated that the presence of VP1 was required to elicit virus-neutralizing antibody activity. However, to date, neutralizing epitopes have been identified only on VP2. Crystallog. studies of a related parvovirus (canine parvovirus) suggested the unique amino-terminal portion of VP1 assumed an internal position within the viral capsid. To det. the position of VP1 in both empty capsids and virions, a fusion protein contg. the unique region of VP1 was expressed. Antisera raised to this protein recognized recombinant empty capsids contg. VP1 and VP2, but not those contg. VP2 alone, in an ELISA. The antisera immunopptd. both recombinant empty capsids and human plasma-derived virions, and agglutinated the latter as shown by immune electron microscopy. The sera contained potent neutralizing activity for virus infectivity in vitro. These data indicate that a portion of the amino terminus of VP1 is located on the virion surface, and this region contains intrinsic neutralizing determinants. The external location of the VP1-specific tail may provide a site for engineered heterologous epitope presentation in novel recombinant vaccines.

L1 ANSWER 3 OF 19 COPYRIGHT 1992 ACS  
AN CA116(1):4844q

TI A second neutralizing epitope of B19 parvovirus implicates the spike region in the immune response  
AU Yoshimoto, Kohji; Rosenfeld, Stephen; Frickhofen, Norbert; Kennedy, Douglas; Hills, Robert; Kajigaya, Sachiko; Young, Neal S.  
CS Cell Biol. Sect., Natl. Heart, Lung, Blood Inst.

LO Bethesda, MD 20892, USA  
SO J. Virol., 65(12), 7056-60  
SC 15-2 (Immunochemistry)  
DT J

CO JOVIAM  
IS 0022-538X  
PY 1991  
LA Eng

AB The authors used 18 monoclonal antibodies against B19 parvovirus to identify neutralizing epitopes on the viral capsid. Of the 18 antibodies, 9 had in vitro neutralizing activity in a bone marrow colony culture assay. The overlapping polypeptide fragments spanning the B19 structural proteins were produced in a pMAL-c Escherichia coli expression system and used to investigate the binding sites of the neutralizing antibodies. One of the nine neutralizing antibodies reacted with both VP1 and VP2 capsid proteins and a single polypeptide fragment on an immunoblot, identifying a linear neutralizing epitope between amino acids 57 and 77 of the VP2 capsid protein. Eight of nine neutralizing antibodies failed to react with either of the capsid proteins or any polypeptide fragments, despite reactivities with intact virions in a RIA, suggesting that addnl. conformationally dependent neutralizing epitopes exist.

L1 ANSWER 4 OF 19 COPYRIGHT 1992 ACS  
AN CA115(19):204724s

TI Induction by some protein kinase inhibitors of differentiation of a mouse megakaryoblastic cell line established by coinfection with Abelson murine leukemia virus and recombinant SV40 retrovirus  
AU Honma, Yoshio; Okabe-Kado, Junko; Kasukabe, Takashi; Hozumi, Motoo;

Kajigaya, Sachiko; Saito, Yoshio; Akita, Yasuhiro  
 Best Available Copy  
 Dep. Chemother., Saitama Cancer Cent. Res. Inst.  
 Ina 362, Japan  
 Cancer Res., 51(17), 4649-55  
 14-1 (Mammalian Pathological Biochemistry)  
 J  
 CNREA8  
 0008-5472  
 1991  
 Eng  
 Mouse C1 line cells are megakaryoblastic cells established by  
 coinfection of Abelson murine leukemia virus and recombinant simian  
 virus 40. This study examined the effects of various compounds on growth  
 and differentiation of these cells. Megakaryocytic differentiation  
 of C1 cells was not induced by cytokines that stimulate  
 megakaryocyte maturation of normal progenitor cells, such as  
 interleukin 3 and 6 and granulocyte-macrophage colony-stimulating  
 factor. However, the cells were induced to differentiate into  
 megakaryocytes by treatment with some protein kinase inhibitors. The  
 inhibition of v-abl tyrosine kinase activity preceded induction of  
 differentiation of the cells treated with tyrosine kinase inhibitors  
 such as genistein, herbimycin A, and erbstatin. Treatment of C1  
 cells with a v-abl antisense oligomer inhibited their proliferation  
 and induced acetyl-cholinesterase activity, a typical marker of  
 megakaryocytic differentiation. These results suggest that  
 inhibition of v-abl function is associated with induction of  
 megakaryocytic differentiation of C1 cells. Among the compounds  
 tested, 1-(5-isoquinolinesulfonyl)-2-methylpiperazine (H-7), a  
 potent inhibitor of cyclic nucleotide-dependent and  
 Ca<sup>2+</sup>-phospholipid-dependent (protein kinase C) protein kinases, was  
 the most potent inducer of differentiation of C1 cells. However, the  
 differentiation-inducing effect of H-7 was unlikely to be mediated  
 through inhibition of protein kinase C or cyclic  
 nucleotide-dependent kinases, because other types of inhibitors of  
 these kinases were not effective, and a protein kinase activator  
 (phorbol ester) induced differentiation of C1 cells. Moreover,  
 neither v-abl mRNA expression nor v-abl kinase activity in C1 cells  
 was affected by treatment with H-7. These findings indicate that  
 induction of megakaryocytic differentiation by H-7 is not related to  
 inhibition of v-abl kinase, but rather to some novel function of  
 H-7.

ANSWER 5 OF 19 COPYRIGHT 1992 ACS  
 CA115(15):154634q  
 Preliminary x-ray crystallographic investigation of human parvovirus  
 B19  
 Agbandje, Mavis; McKenna, Robert; Rossmann, Michael G.; Kajigaya,  
 Sachiko; Young, Neal S.  
 Dep. Biol. Sci., Purdue Univ.  
 West Lafayette, IN 47907, USA  
 Virology, 184(1), 170-4  
 10-1 (Microbial Biochemistry)  
 6, 75  
 J  
 VIRLAX  
 0042-6822  
 1991  
 Eng  
 Crystals that diffract x rays to at least 8 .ANG. resolu. were grown  
 from human B19 parvovirus empty capsids. These particles consist of  
 VP-2 derived from a baculovirus expression system. This is possibly  
 the first time that a self-assembled empty viral capsid, grown in  
 other than normal host cells, has been crystd. Partial x-ray  
 diffraction data have been collected using synchrotron radiation.  
 The space group is P2<sub>1</sub>3 with a = 362 .ANG.. The particle position in  
 the crystal cell is given, at least roughly, from packing

L1 ANSWER 6 OF 19 COPYRIGHT 1992 ACS  
 AN CA115(13):133520j  
 TI Self-assembled B19 parvovirus capsids, produced in a baculovirus system, are antigenically and immunogenically similar to native virions  
 AU Kajigaya, Sachiko; Fujii, Hiroyuki; Field, Anne; Anderson, Stacie; Rosenfeld, Stephen; Anderson, Larry J.; Shimada, Takashi; Young, Neal S.  
 CS Clin. Hematol. Branch, Natl. Heart, Lung, Blood Inst.  
 LO Bethesda, MD 20892, USA  
 SO Proc. Natl. Acad. Sci. U. S. A., 88(11), 4646-50  
 SC 15-2 (Immunochemistry)  
 SX 10  
 DT J  
 CO PNASA6  
 IS 0027-8424  
 PY 1991  
 LA Eng  
 AB B19 parvovirus is pathogenic in humans, causing fifth disease, transient aplastic crisis, some cases of hydrops fetalis, and acquired pure red cell aplasia. Efforts to develop serol. assays and vaccine development have been hampered by the virus's extreme tropism for human bone marrow and the absence of a convenient culture system. Recombinants were constructed contg. either the major (VP2) or minor (VP1) structural proteins of B19 in a baculovirus-based plasmid, from which the polyhedrin gene had been deleted; these recombinant plasmids were used to generate recombinant infectious baculovirus. Subsequent infection of insect cells in vitro resulted in high-level expression of either B19VP1 or VP2. Parvovirus capsids were obtained by self-assembly in cell cultures coinfectd with either VP1- and VP2-contg. baculoviruses or, surprisingly, VP2-contg. baculoviruses alone. Empty B19 capsids composed of VP1 and VP2 could replace serum virus as a source of antigen in a conventional immunoassay for detection of either IgG or IgM antiparvovirus antibodies in human serum. Immunization of rabbits with capsids composed of VP1 and VP2 resulted in prodn. of antisera that recognized serum parvovirus on immunoblot and neutralized parvovirus infectivity for human erythroid progenitor cells. Thus, baculovirus-derived parvovirus antigen can substitute for scarce viral antigen in immunoassays and should be suitable as a human vaccine.

L1 ANSWER 7 OF 19 COPYRIGHT 1992 ACS  
 AN CA113(13):113342h  
 TI A genetically engineered cell line that produces empty capsids of human parvovirus B19  
 AU Kajigaya, Sachiko; Frickhofen, Norbert; Kurtzman, Gary; Shimada, Takashi; Young, Neal S.; Field, Anne  
 CS Clin. Hematol. Branch, NHLBI  
 LO Bethesda, MD 20892, USA  
 SO Vaccines 90: Mod. Approaches New Vaccines Incl. Prev. AIDS, [Conf.], 7th, Meeting Date 1989, 63-8. Edited by: Brown, Fred. Cold Spring Harbor Lab.: Cold Spring Harbor, N. Y.  
 SC 15-2 (Immunochemistry)  
 DT C  
 CO S6UPAE  
 PY 1990  
 LA Eng  
 AB A 3-11-5 cell line that stably produces B19 parvovirus empty capsids was established. Empty capsid prodn. is equal to or greater than virion prodn. by infected bone marrow cells, estd. at 1000-2000 capsids/cell. The growth of cells was not diminished by capsid prodn. In capture immunoassay, 3-11-5 lysate was equiv. to serum contg. virus for the detection of IgG and IgM antibodies. This cell

line will be useful for the development of clin. anti B19 parvovirus antibody assays, as it should provide an unlimited supply of B19 antigen. The 3-11-5 cells are potentially useful in the development of a vaccine and a packaging cell line for gene therapy.

L1 ANSWER 8 OF 19 COPYRIGHT 1992 ACS  
AN CA113(7):55470k  
TI Establishment of cell strain producing empty capsid of parvovirus B19  
AU Kajigaya, Sachiko  
CS Natl. Health Inst.  
LO Bethesda, MD 20892, USA  
SO Jikken Igaku, 8(8), 969-72  
SC 10-0 (Microbial Biochemistry)  
SX 3  
DT J  
CO JIIGEF  
IS 0288-5514  
PY 1990  
LA Japan  
AB A review with 6 refs. on the properties and characteristics of parvovirus B19, establishment of a cell line producing B19-empty capsid by genetic engineering technol., detection for B19-capsid protein, and assembly of the B19-capsid protein.

L1 ANSWER 9 OF 19 COPYRIGHT 1992 ACS  
AN CA112(1):6051v  
TI A genetically engineered cell line that produces empty capsids of B19 (human) parvovirus  
AU Kajigaya, Sachiko; Shimada, Takashi; Fujita, Shinsuke; Young, Neal S.  
CS Cell Biol. Sect., Natl. Heart, Lung, Blood Inst.  
LO Bethesda, MD 20892, USA  
SO Proc. Natl. Acad. Sci. U. S. A., 86(19), 7601-5  
SC 16-9 (Fermentation and Bioindustrial Chemistry)  
SX 3, 14  
DT J  
CO PNASA6  
IS 0027-8424  
PY 1989  
LA Eng  
AB The right half of the cloned B19 genome and a minigene derived from the human dihydrofolate reductase gene (DHFR) were cotransfected into dhfr- Chinese hamster ovary cells and selected clones were screened by RNA anal.; after amplification in methotrexate, clones were tested for capsid protein expression. A cell line, designated 3-11-5, stably expressed nearly full-length transcripts for the 2 capsid proteins. These cells produced the major and minor structural protein species in natural proportions that self-assembled into virion capsids. Capsids from 3-11-5 cells could be sepd. from virions by sucrose gradient sedimentation and had the d. on CsCl isopycnic sedimentation of empty parvovirus capsids. Capsid protein was present in both nuclei and cytoplasm on immunofluorescence study but fractionated with the cytosol on purifn. Empty capsid prodn. was equal to or greater than virion prodn. by infected bone-marrow cells, 1000-2000 capsids/cell, but cell growth was not diminished by capsid prodn. This cell line will be useful in developing practical assays for B19 parvovirus antibody and a vaccine for the virus, as well as potentially serving as a packaging cell line for gene therapy.

L1 ANSWER 10 OF 19 COPYRIGHT 1992 ACS  
AN CA109(17):143475p  
TI The gene encoding the nonstructural protein of B19 (human) parvovirus may be lethal in transfected cells  
AU Ozawa, Keiya; Ayub, Jamshed; Kajigaya, Sachiko; Shimada, Takashi;

CS Clin. Hematol. Branch, Natl. Heart, Lung, Blood Inst.  
LO Bethesda, MD 20892, USA  
SO J. Virol., 62(8), 2884-9  
SC 3-2 (Biochemical Genetics)  
SX 10  
DT J  
CO JOVIAM  
IS 0022-538X  
PY 1988  
LA Eng  
AB

The B19 parvovirus is a cause of bone marrow failure in humans. B19 is toxic to erythroid progenitor cells in vitro. Viral products possibly responsible for toxicity were explored by transfection of cloned B19 genome into HeLa cells. The nonstructural (NS) protein was detected in cells 30 h after transfection. Plasmids contg. the B19 genome were transfected with selectable marker genes in stable transformation assays. Plasmids that contained the left side of the B19 genome, which encodes the NS protein of the virus, inhibited antibiotic-resistant colony formation. Transformation occurred when NS protein expression was blocked by mutation. Suppression of transformation by NS protein was not tissue specific, suggesting a role for NS protein in toxicity for nonpermissive cells without parvovirus replication or virion accumulation.

L1 ANSWER 11 OF 19 COPYRIGHT 1992 ACS

AN CA107(25):234524d

TI Effects of recombinant murine granulocyte colony-stimulating factor on granulocyte-macrophage and blast colony formation

AU Suda, Toshio; Suda, Junko; Kajigaya, Sachiko; Nagata, Shigekazu; Asano, Shigetaka; Saito, Masaki; Miura, Yasusada

CS Inst. Hematol., Jichi Med. Sch.

LO Minamikawachi 329-04, Japan

SO Exp. Hematol. (N. Y.), 15(9), 958-65

SC 15-5 (Immunochemistry)

DT J

CO EXHMA6

IS 0301-472X

PY 1987

LA Eng

AB In order to define the in vitro hemopoietic activity of murine recombinant (r) granulocyte colony-stimulating factor (G-CSF), murine hemopoietic culture systems of normal bone marrow cells, fetal liver cells, and spleen cells of 5-fluorouracil (FU)-treated mice were used. rG-CSF supported only neutrophil and/or macrophage colony formation by normal bone marrow cells. It did not enhance the formation of erythroid bursts in the fetal liver cell assay, but interleukin-3 (IL-3) did. Paradoxically, rG-CSF could support the colony formation of multilineage colonies as well as blast colonies from the spleen cells of 5-FU-treated mice, which r-granulocyte-macrophage (GM)-CSF and r-erythropoietin (Ep) did not. When blast colonies, formed in the presence of G-CSF, were replated to dishes contg. IL-3, they were able to differentiate along multilineage pathways. However, when they were replated to dishes contg. rG-CSF, they could differentiate only into neutrophils and macrophages. Single cells transferred from blast colonies formed only neutrophil-macrophage colonies. Thus, rG-CSF had a direct effect on the growth and development of GM progenitors at a late stage and an effect on multipotential hemopoietic precursors.

L1 ANSWER 12 OF 19 COPYRIGHT 1992 ACS

AN CA105(21):189160c

TI A recombinant murine granulocyte/macrophage (GM) colony-stimulating factor derived from an inducer T cell line (IHS.5). Functional restriction to GM progenitor cells

AU Kajigaya, Sachiko; Suda, Toshio; Suda, Junko; Saito, Masaki; Miura,

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Sudo, Tetsuo  
 CS Div. Hematol., Jichi Med. Sch.  
 LO Japan  
 SO J. Exp. Med., 164(4), 1102-13  
 SC 1S-5 (Immunochemistry)  
 DT J  
 CO JEMEAU  
 IS 0022-1007  
 PY 1986  
 LA Eng  
 AB The cDNA for the murine granulocyte/macrophage colony-stimulating factor (GM-CSF) was cloned from a cDNA library obtained from a murine T cell line, IH5.5, by using 2 synthetic probes that encoded 2 parts of the GM-CSF from murine lung. The cDNA inserted into the plasmid vector pcDV1 was transfected into monkey COS-1 cells and the conditioned medium was used to investigate the hemopoietic activities of the resultant product, recombinant GM-CSF (rGM-CSF), by means of various colony assays. RGM-CSF stimulated only neutrophil/macrophage colonies in the cultures of murine normal bone marrow and fetal liver cells. No other colony stimulating activities (CSA) were seen in the prepn. RGM-CSF could not support colony formation of 5-fluorouracil-treated mouse spleen cells, in which only the primitive population of stem cells survived. However, after culture of these cells with pokeweed mitogen-spleen cell-conditioned medium, the colonies consisting of blast cells were formed. These blast cells could now be induced to form neutrophil/macrophage colonies in the presence of rGM-CSF. Pure neutrophil colonies, pure macrophage colonies, as well as mixed neutrophil/macrophage colonies, were formed from these single blast cells in the presence of rGM-CSF by micromanipulation. RGM-CSF did not act on pluripotent hemopoietic stem cells, but did act directly and selectively on neutrophil/macrophage progenitors. Moreover, striking heterogeneities were noted in the size of the colonies and the proportion of components. GM-CSF is, therefore, considered to play a noninstructive role in the differentiation of the GM pathway.

L1 ANSWER 13 OF 19 COPYRIGHT 1992 ACS  
 AN CA105(21):184724e  
 TI Erythropoietic activity in the medium conditioned by mouse spleen cells or 2E10.4.13 cells detected by erythroid colony formation of mouse fetal liver cells in serum-free soft agar cultures  
 AU Kajigaya, Sachiko; Kubota, Kazuo; Minato, Nagahiro; Suda, Toshio; Kano, Shogo; Miura, Yasusada  
 CS Inst. Hematol., Jichi Med. Sch.  
 LO Japan  
 SO Jichi Ika Daigaku Kiyo, 8, 55-64  
 SC 2-9 (Mammalian Hormones)  
 DT J  
 CO JIDKE2  
 PY 1985  
 LA Japan  
 AB A serum-free soft agar culture system was established for colony formation by mouse fetal liver cells. Fetal liver cells from ICR mice were cultured in Iscove's medium supplemented with 0.3% agar, bovine serum albumin, transferrin, cholesterol, L-.alpha.-phosphatidylcholine, 10-4M mercaptoethanol, and a hemopoietic factor. After 2 days of incubation, erythroid colonies were scored after Hb staining. The plating efficiency for the serum-free cultures was .apprx.70% of that for the serum-supplemented cultures. A max. colony formation was obtained at a concn. of 80 milliunits/mL erythropoietin (Ep) [11096-26-7] in the serum-free cultures as well as in the serum-supplemented cultures. The serum-free culture system makes it possible to detect a very low concn. of Ep, because no erythroid colonies were obsd. without the addn. of exogenous Ep. This system was used to investigate whether Ep was contained in the



media conditioned by phorbol myristate acetate-stimulated 2E10.4.13 cells. The 2E10.4.13 cell line has phenotypical as well as genotypical features of inducer T-cell. Both conditioned media stimulated erythroid colony formation. A study using a Sephadex G-100 column demonstrated that the apparent mol. wt. of the active substances in these conditioned media were similar and were .apprx.40,000-45,000 daltons. These Ep-like factors showed different peaks from erythropoietic activities in human urine, human serum, and mouse serum sepd. by Sephadex G-100 column. This difference might be due to altered modification, such as glycosylation, of the protein.

L1 ANSWER 14 OF 19 COPYRIGHT 1992 ACS

AN CA103(9):69605p

TI A murine cell line (2E10.4.13) produces five hemopoietic stimulators, and interleukin-2 and interleukin-3

AU Kajigaya, Sachiko; Kubota, Kazuo; Minato, Nagahiro; Sudo, Tetsuo; Hatake, Kiyohiko; Iizuka, Masahiko; Kobayashi, Shigeyasu; Saito, Masaki; Kano, Shogo; Miura, Yasusada

CS Inst. Hematol., Jichi Med. Sch.

LO Kamakura 248, Japan

SO Cell Struct. Funct., 10(2), 121-31

SC 15-5 (Immunocytochemistry)

DT J

CO CSFUDY

IS 0386-7196

PY 1985

LA Eng

AB An interleukin-2 (IL-2)-independent murine lymphocyte clone (2E10.4.13) with Thy1+Ly1+2-T200+ phenotype was sepd. from the original IL-2-dependent natural killer (NK) cell line (PEC-1). Erythroid burst-promoting activity (BPA), erythropoietin (Ep), granulocyte/macrophage, megakaryocyte and eosinophil colony-stimulating factors (GM-, MK- and Eo-CSF), IL-2 and Interleukin-3 (IL-3) were produced when these cells were stimulated with phorbol myristate acetate (PMA). When the conditioned medium was run through ion-exchange HPLC, BPA, Ep, GM-CSF, MK-CSF, and Eo-CSF were eluted in the same region as IL-3. In contrast, MK-CSF, much of the GM-CSF and half of the Eo-CSF were eluted in a distinct region where no IL-3 was detected. Chem. analyses of the hemopoietic factors derived from a single T inducer clone indicated that all the hemopoietic activities were assocd. with IL-3 activity. Some CSF activities (GM-, MK- and Eo-CSF) also could be mediated by the distinct mols. from IL-3, evidence that heterogeneous mols. are responsible for CSF activity.

L1 ANSWER 15 OF 19 COPYRIGHT 1992 ACS

AN CA102(21):182092m

TI Isolation and characterization of defective-interfering particles of poliovirus Sabin 1 strain

AU Kajigaya, Sachiko; Arakawa, Hiroshi; Kuge, Shusuke; Koi, Toshitaka; Imura, Nobumasa; Nomoto, Akio

CS Sch. Pharm. Sci., Kitasato Univ.

LO Tokyo 108, Japan

SO Virology, 142(2), 307-16

SC 10-1 (Microbial Biochemistry)

DT J

CO VIRLAX

IS 0042-6822

PY 1985

LA Eng

AB Defective-interfering (DI) particles of the Sabin strain of type 1 poliovirus were generated on serial high m.o.i. passaging. The deletions, measured by agarose gel electrophoresis, appeared to comprise .apprx.10% of the total genome. Anal. of the RNAs, after

digestion with RNase T1, by 2-dimensional polyacrylamide gel electrophoresis revealed that the locations of the deleted genome regions were similar to those of the DI particles of the Mahoney strain of type 1 poliovirus. Taking the known nucleotide sequences of the total genome and large RNase T1-resistant oligonucleotides into account, the deletions of almost all DI RNAs were found to exist between nucleotide positions 1307 and 2630, a genome region encoding capsid polypeptides VP2, VP3, and VP1. In cells coinfectd with the purified DI particles and the Sabin strain of type 2 or type 3 poliovirus, particles contg. the DI genomes were effectively produced. Apparently, encapsidation signals are conserved in all 3 serotypes of polioviruses. However, only a very small amt. of similar DI particles appeared to be produced in cells coinfectd with coxsackie virus B1, although the genomes of polioviruses and coxsackie viruses have common sequences and therefore these viruses are considered to have arisen from a common ancestor. These data may suggest differences in encapsidation signals between polioviruses and coxsackie viruses.

L1 ANSWER 16 OF 19 COPYRIGHT 1992 ACS

AN CA101(15):128158d

TI Inhibitory activity on murine granulocytic colony formation of bone marrow cell-conditioned medium obtained from colony-stimulating factor-producing tumor-bearing nude mice

AU Motoyoshi, Kazuo; Ishizaka, Yukihiro; Ikeda, Kazuma; Kajigaya, Sachiko; Hatake, Kiyohiko; Shionoya, Shigeru; Saito, Masaki; Miura, Yasusada

CS Inst. Hematol., Jichi Med. Sch.

LO 329-04, Japan

SO Cancer Res., 44(8), 3313-16

SC 14-1 (Mammalian Pathological Biochemistry)

DT J

CO CNREAB

IS 0008-5472

PY 1984

LA Eng

AB The effects of bone marrow-conditioned medium obtained from colony-stimulating factor-producing tumor-bearing nude mice (G-BM-CM) on mouse and human granulocyte-macrophage colony formation and mouse erythroid colony and burst formation were studied. Addn. of G-BM-CM into the mouse granulocyte-macrophage colony-forming system contg. colony-stimulating activity more strongly inhibited granulocyte colony formation than mixed granulocyte-macrophage and macrophage colony formation, while it did not change the no. of granulocyte colonies formed by human bone marrow cells stimulated by human granulocyte colony-stimulating activity. Addn. of G-BM-CM slightly increased mouse erythroid colony and burst nos. when it was added into an erythroid colony-forming system stimulated by erythropoietin, and into the erythroid burst-forming system stimulated by erythropoietin and 7% spleen cell-conditioned medium. Apparently, G-BM-CM mainly blocked commitment of mouse granulocyte-macrophage colony-forming cells to granulocytic progeny.

L1 ANSWER 17 OF 19 COPYRIGHT 1992 ACS

AN CA100(13):97366t

TI Clonal growth of human acute myeloid leukemia cells (ML-1 and HL-60) in serum-free agar medium

AU Taketazu, Fumitoshi; Kubota, Kazuo; Kajigaya, Sachiko; Shionoya, Shigeru; Motoyoshi, Kazuo; Saito, Masaki; Takaku, Fumimaro; Miura, Yasusada

CS Inst. Hematol., Jichi Med. Sch.

LO Tochigi 329-04, Japan

SO Cancer Res., 44(2), 531-5

SC 2-9 (Mammalian Hormones)

SX 15

DT J

CO CNREAB

IS 0008-5472  
PY 1984  
LA Eng  
AB Human acute myeloid leukemia (ML-1 and HL-60) cells grew continuously in the serum-free liq. medium supplemented with human transferrin and bovine insulin. Both ML-1 and HL-60 cells formed clusters and colonies in the serum-free agar medium supplemented with bovine serum albumin, human transferrin, cholesterol, and L-.alpha.-phosphatidylcholine. Medium conditioned by phytohemagglutinin-stimulated leukocytes prepd. in the absence of serum had 3 types of colony-stimulating factor [62683-29-8] on normal human bone marrow cells. When fetal calf serum was present, medium conditioned by phytohemagglutinin-stimulated leukocytes stimulated the clonal growth of HL-60 cells at the lower concn. However, it inhibited that of ML-1 cells. In contrast, under serum-free conditions, medium conditioned by phytohemagglutinin-stimulated leukocytes promoted the clonal growth of both ML-1 and HL-60 cells at the lower concns. The study using a Sephadex G-200 column revealed that, in the serum-supplemented cultures, HL-60 cells responded to 1 of 3 colony-stimulating factors and to an activity with mol. wt. .apprx.12,000, while ML-1 cells responded only to an activity with mol. wt. .apprx.12,000. In the serum-free cultures, both ML-1 and HL-60 cells were stimulated by activities with mol. wts. of 62,000 and 54,000, resp. Thus, the detn. of growth factors for cell lines is dependent on culture conditions, particularly on serum components. There is a heterogeneity of ML-1 and HL-60 cells in response to the growth factors. There is potential importance of demonstration of heterogeneity among different cell lines in establishing requirements for different stages of differentiation.

L1 ANSWER 18 OF 19 COPYRIGHT 1992 ACS  
AN CA98(11):84167u  
TI Stimulation of erythropoiesis in teratocarcinoma cells by erythropoietin and "Friend inducers"  
AU Kajigaya, Sachiko; Miura, Yasusada  
CS Inst. Hematol., Jichi Med. Sch.  
LO Minamikawachi 329-04, Japan  
SO Exp. Cell Res., 142(2), 468-71  
SC 2-9 (Mammalian Hormones)  
DT J  
CO ECREAL  
IS 0014-4827  
PY 1982  
LA Eng  
AB Murine teratocarcinoma cells (PCC3/A1) formed erythroid cells in the form of blood islands when they were grown in organ culture. Addn. of dimethyl sulfoxide (DMSO) [67-68-5], N,N'-dimethylacetamide [127-19-5], and erythropoietin [11096-26-7] enhanced the formation of blood islands. An additive stimulatory effect was obsd. when explants were incubated with DMSO and erythropoietin. In all of these cultures, the formed erythroblasts showed the characteristics of primitive erythroid cells, regardless of the nature of treatment. Small, enucleated red cells were occasionally obsd. These results were compared with the characteristics of erythropoiesis in normal adults, in embryos, and in murine erythroleukemia.

L1 ANSWER 19 OF 19 COPYRIGHT 1992 ACS  
AN CA92(3):18666f  
TI Possible point mutation sites in LSc, 2ab poliovirus RNA and a protein covalently linked to the 5'-terminus  
AU Nomoto, Akio; Kajigaya, Sachiko; Suzuki, Keiko; Imura, Nobumasa  
CS Sch. Pharm. Sci., Kitasato Univ.  
LO Tokyo 108, Japan  
SO J. Gen. Virol., 45(Pt. 1), 107-17